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Visual Search in the Detection of Retinal Injury: A Feasibility Study

Thomas Kuyk
TASC, Inc.

Lei Liu
The University of Alabama at Birmingham

Elizabeth Belleau
Human Effectiveness Directorate
Bioeffects Division
Optical Radiation Bioeffects Branch

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Air Force Research Laboratory
711th Human Performance Wing
Human Effectiveness Directorate
Bioeffects Division
Optical Radiation Bioeffects Branch
JBSA Fort Sam Houston TX 78234

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LEON N. McLIN, JR., DR-III, DAF
Work Unit Manager
711 HPW/ RHDO

POLHAMUS.GARRETT.D.1175839484

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GARRETT D. POLHAMUS, DR-IV, DAF
Chief, Bioeffects Division
Human Effectiveness Directorate
711th Human Performance Wing
Air Force Research Laboratory

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711th Human Performance Wing
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14. ABSTRACT

A feasibility study was conducted to determine if small areas of vision loss (scotoma) on the order of 1° in the central 10-20° of the visual field could be detected using a visual feature search paradigm. Scotoma of varying size and location were simulated in subjects with normal vision using a gaze contingent eye tracking system. Response time (RT) for target detection was measured. Two experiments were completed. Results of the first experiment with experienced observers indicated 1.1° and 1.6° scotoma could be detected based on RT differences in the central 10° and 20° of the visual field, respectively when the scotoma were located adjacent to the target. Grid size, item size and item density to achieve detection were varied and results were used to set parameters for the second experiment. In experiment 2, naive observers were tested and scotoma locations were fixed. The test situation was similar to one that might be used for a clinical evaluation. The results indicated that with an 11 x 11 grid, a 1.1° scotoma could be detected in the central 10° (out to 6° eccentricity). When scotoma were located more peripherally (out to 11° eccentricity), minimum detectable scotoma size increased to 1.6° and grid size had to be increased to 13 x 13. The positive results suggest the feature search paradigm has sufficient merit as a method to detect small central scotoma to warrant further study. Directions for future research and ways to improve the methodology and speed of data collection are discussed.

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1.0 INTRODUCTION

The use of lasers on the battlefield continues to grow as increasingly sophisticated systems are fielded and new purposes for their use are discovered. For many years, lasers have been widely used for range finding, target designation, and illumination to guide munitions to targets. More recently, lasers operating in the visible range have been used to dazzle adversaries with bright light or to signal warning. Powerful lasers are also being developed to jam sensors in ground vehicles and aircraft or to disable and destroy them.[1-2] The majority of lasers in use operate at visible and near-infrared (NIR) wavelengths of the electromagnetic spectrum. The retina is very susceptible to injury at these wavelengths because the optics of the eye focuses these wavelengths upon it. Since many military laser systems are quite powerful, injury due to exposure can occur with even very brief exposures. The outcome of an exposure can range from temporary visual effects such as glare and flashblindness to retinal damage and permanent visual impairment.

The wide-spread use of lasers increases the probability of injury to the eye. This is evidenced by the increase in laser-related injuries that accompanied the ubiquitous use of visible lasers by ground personnel in Iraq and Afghanistan over the past several years. The Air Force has also reported an increase in exposures to aircrew from laser pointers aimed at aircraft during approach and landing with 69 incidents reported to the Department of Defense laser hotline in 2012.[3] Some events in the past resulted in aircrew being evacuated outside the theatre of operations in order to determine if injury had occurred. Similarly, the US Coast Guard has reported an increase in laser incidents involving helicopter aircrew and has adopted a policy of grounding affected individuals until they have had an eye examination.[4] On the civilian side, the Federal Aviation Administration has reported a dramatic increase in laser incidents over the past decade with approximately 3500 reported in 2012.[5] Blinding laser weapons have been prohibited by international treatise; however, that does not mean that adversaries will not use them in the future.

Retinal lesions caused by laser exposure can be of different types, affect ocular structures differentially, and be of varying size depending on the laser wavelength and the exposure duration.[6] Lesions may be bilateral or unilateral depending on the angle of incidence of the laser and the direction of gaze. Laser injuries that are visually significant are usually accompanied by immediate and severe disruptions of vision.[7] It makes intuitive sense that loss of vision can be catastrophic in combat and flight situations. Simulation studies show that even small lesions in the fovea have the potential to cause severe disruptions of vision and degradation in the performance of tasks such as visual search and tracking.[8-10] Lesions outside of the fovea may or may not be immediately noticed unless they are extensive in size. Lesions that are small and localized and scattered across the retina outside the fovea may be particularly difficult to detect.[11] Detecting any lesion is important since the long-term visual consequences and actual extent of the damage at the time of exposure are not likely to be known.[6, 7] The current Air Force Laser Injury Guidebook expressly states that: "The flight surgeon should approach a laser eye injury as a potentially serious injury." [12]

A sensitive psychophysical test could prove useful for early screening of suspected injury outside the fovea, for later verification that an injury has occurred with vision loss, and potentially as a tool for monitoring recovery. However, screening methods that might be used under battlefield conditions to detect small lesions outside the fovea are limited and of questionable validity. The US Army has developed a screening tool called the AIDMAN [13, 14] for this purpose. The current version of the test employs a variety of charts including the Amsler grid, high and low contrast near acuity, and color chart tests. However, the test has not been validated for laser eye injury detection and, to our knowledge, is not currently in use. Furthermore, it focuses almost entirely on assessment of foveal function. The only test in the battery that assesses vision outside the fovea is the Amsler Grid, which evaluates the central 20° of the visual field. However, the Amsler Grid has not been found to be a reliable indicator of visual field loss [15, 16] and is inappropriate for detecting smaller scotoma which can be easily filled in perceptually by the lines on the chart, as demonstrated by Schuchard.[15]

We proposed that a visual feature search task might serve as a tool for screening of laser injuries outside the fovea. The present study was as a feasibility study to determine if relatively small simulated laser lesions within the central 10-20° of the visual field could be detected with a feature search task. Elevations in response times to detect a search target presented at specific retinal locations may suggest potential underlying damage. If this is the case, then individuals with suspected injury could be referred for additional testing in a clinical setting using more sophisticated tools such as fundus photography, flourescein angiograpy, microperimetry, or optical coherence tomography.[12] However, even these tests may not be sensitive enough to diagnose patients with minor injury.[11] It is possible that a visual detection task such as static perimetry might serve that purpose although that remains to be demonstrated and is not the purpose of the present study.

In a feature search task, a target and a set of distractors are presented simultaneously to a subject (see Figure 1). The target differs from the distractors along one visual feature dimension, for example, contrast, color, or size. If the difference is a salient one, the target seems be immediately visible and to "pop out" from the distractors, search speed is fast and is not influenced by the number of distractors (set-size). Such feature search is said to be accomplished by the preattentive system, which extracts basic visual features (color, orientation, size, and so on) in parallel across the visual field, and seems to have unlimited capacity.[17,18] In normal subjects, the detection of the target is typically reported in a few hundreds of milliseconds and does not require an eye movement. In contrast, if the target is not conspicuous, e.g., contrast or color differences between target and distractors are not large enough, or the target and distractors vary along more than one feature dimension (e.g., color and orientation), then the array of items must be serially searched using covert focal attention shift and/or overt eye movements until the target is located and response time (RT) is significantly slower.[17]

In a feature search test, a search area of a given size, for example 10° x 10°, is covered by a rectilinear search grid, for example, 9 x 9. A target and a set of distractors, the stimulus array, are presented simultaneously on some of the grid points to a subject (see Figure 1). Over a series of trials, the target is presented once at every location of the search grid, thus offering the chance to examine the functional integrity of all grid locations in the area of the visual field covered by the search grid. The subject's task is to respond as quickly as possible if the target is present or if no target is present on a trial.

The "pop out" phenomenon of feature search is particularly relevant to laser injury detection because a small retinal lesion may conceal, distort the shape of, or change the luminance of the search target imaged in its vicinity and result in a change in search performance (i.e., an increase in the time required to respond to the target). Our hypothesis is that localized retinal laser injury will disrupt search for salient visual targets imaged on and next to the damaged area and will result in increases in response times (RT) for target detection at and/or near the lesion site. The existence, retinal location, and extent of a parafoveal scotoma can be determined by monitoring trial-by-trial response accuracy and reaction time. Specifically, trials that produce RTs that are significantly longer than the session mean RT or missed responses (a report of target absence in a target-present trial) are likely to have the target falling in or near a scotoma. The selection of a highly salient feature search stimulus ensures that RT for targets imaged on undamaged retinal areas will not be elevated because they are unlikely to be missed. In the case of complete or very significant obscuration, RT will increase because subjects will need to make eye movement(s) to move the scotoma away from the target and "uncover" it, rendering it visible, allowing them to make an accurate response about target presence or absence. Eye movements take time, and the number of saccades made during visual search is highly correlated with reaction time.[19, 20] For less than total obscuration of the target, additional eye movements may be needed or RT will be increased because target saliency is decreased and more time is required for the target to be recognized.[21] The impetus for this study was based on studies of feature search in visually impaired adults with central and/or peripheral visual field loss.[22-24] Those studies found that persons with visual field loss, even severe loss, could perform a feature search task, but did so more slowly than persons with normal vision.[22, 23] In addition, plots of RT for hits as a function of target location on the search grid revealed regions of elevated RT that roughly corresponded to areas of visual field loss.[24]

Since a visual search paradigm had not previously been used for the purpose of retinal laser injury detection, relationships between grid size, search item size, and scotoma size needed to be established to determine what scotoma size can be detected with what grid size/item size combination. Since the average size of laser lesions caused by military and industrial accidents is not specifically known, we used data on lesions resulting from photocoagulation therapy as a guide to establish lesion sizes that would be tested. Laser lesions from photocoagulation therapy vary in size and severity although moderate lesions generally range in size from approximately 300-600 um in greatest diameter, which corresponds to approximately 1-2 degrees of visual angle.[25, 26] An initial experiment using experienced observers was completed (also some pilot data was collected prior to the experiment) to determine some of the relationships between search area, grid size, search stimulus size and density, and visual feature types and to establish parameters that were used in a second experiment. The second experiment used naïve observers under test conditions that more closely reflected a real-life laser injury scenario. Although the primary outcome measure was RT for target detection, the simulation study provided eye movement information; data which are not likely to be available in real scotoma detection tests. Since eye movements may provide insights into search behavior in the presence of small parafoveal scotoma, some of these data were also analyzed.

Procedure-wise, feature search is similar to a single-intensity suprathreshold screening program in static perimetry. Although the advantage of feature search over static perimetry in detecting areas of vision loss has not been established, with respect to detecting small scotoma, feature search has several potential advantages over perimetry. First, feature search is a suprathreshold task with a built-in decision reference. The detection of the target is made against a set of constantly-present, clearly defined, suprathreshold distractors. Static perimetry, though appearing to be a simpler task, does not have a physical reference for decision making and is highly influenced by the fluctuation of the subject's internal noise. Therefore, from the psychophysical point of view, the performance of feature search task should be much more robust than that of the typical static perimetry task. Second, static perimetry is a contrast detection task. Unless the lesion reduces test spot contrast to a subthreshold level, the lesion will not be detected. In comparison, feature search is an automated, parallel discrimination task. Any aspect of the lesion that reduces the differences between the target and distracters can result in detectable performance changes. For example, a target only partially obscured by the scotoma may not be distinguished from the distracters because of the altered total luminance, area or shape, and lesion presence will be characterized by longer RT or increased response error. Third, static perimetry typically uses a very small light spot to probe the visual field. For example, typical single intensity suprathreshold screening using Humphrey Field Analyzer is done with the Goldmann III stimulus, which is 23.4 arc minutes in size. As eccentricity of the test location increases so does the distance between neighboring test locations. From a pure probabilistic point of view, a smaller stimulus has a smaller chance to spatially overlap with a small scotoma, and thus a smaller chance to detect it. Because feature search is based on the perceived difference between the target and the distractors, the spatial extent of these search items can be much larger. Larger search items increase the coverage of the field and thus have the potential to detect smaller scotoma.

While the main goal of the study was to determine feasibility of visual search for laser injury screening, it also has the potential to fill a knowledge gap about the effects of small scotoma outside the fovea on visual function. There is currently a fairly large body of literature on the effects of foveal and large parafoveal scotoma and general peripheral field restrictions, both simulated and in diseased eyes, on behaviors ranging from visual search, tracking, to navigation and reading.[8-10, 27-29] In contrast, and to our knowledge, there have been no studies of the effects on vision of small scotoma in the central 20°.

2.0 METHODS AND RESULTS

2.1 Subjects

Two experiments were conducted. For experiment 1, five subjects (3 males, 2 females) who were experienced psychophysical observers participated. All subjects had distance visual acuity of 20/25 or better in each eye (corrected with contacts or uncorrected), normal visual fields, no self-reported vision problems, and were not taking any medication that affected vision. All but one subject had normal color vision. Subjects ranged in age from 23 to 65 years with a sample mean of 41 years. For experiment 2, nine individuals (7 males, 2 females), who were inexperienced psychophysical observers and naïve to the purpose of the study, participated. All had distance visual acuity of 20/25 in each eye (corrected with contacts or uncorrected), normal visual fields, no self-reported vision problems, and were not taking any medication that affected vision. All but one subject had normal color vision. Subjects ranged in age from 20 to 35 years with a sample mean of 25 years. The voluntary informed consent of all subjects was obtained as required by AFI 40-4021. The research was approved by the Wright Patterson Institutional Review Board.

2.2 Apparatus

The primary piece of equipment was an EyeLink II eye tracking system (SR Research, Ltd, Kanata Ontario, Canada). The system consisted of a head-born infrared camera based eye tracker, a host computer and software that controlled the eye tracker, a second, display computer, software, and monitor (Sony model GDM F520, screen resolution 1600 x 1200 pixels) which generated and displayed the visual stimuli. The system was set up in a gaze contingent configuration. In this format, the eye tracking system knows exactly where the eyes are looking on the display. This allowed a small region in the visual field of view to be created that simulated an area of vision loss, i.e., a laser lesion. In that region of simulated loss, no visual information was displayed on the stimulus monitor. The region of no vision moved as the eye moved, as would be the case with a real scotoma caused by a retinal burn or eye disease (e.g. glaucoma). The experiments were done binocularly, since the eye tracker used calibration data from both eyes to place the scotoma. In a real-life situation testing may need to be monocular since variations in viewing situations including interference by equipment and eye wear may result in monocular lesions. Viewing distance was 57 cm.

The two computers were linked through an Ethernet cable so that information could be exchanged between them at an effective delay of ~2 milliseconds (ms). The eye tracker was an essential component of a gaze-contingent display psychophysical paradigm, in which the eye tracker provides 500 sets of eye position data/second to the display computer that uses the most recent eye position data to update the stimulus image to be displayed in the next video frame of the monitor. Specifically, the display computer placed a transparency mask, the simulated sctotoma, on the search image at a location with a fixed geometric relationship to the current eye position and then sent the modified image to the video buffer of the video card for display in the next frame. The transparency profile of the mask ranged from completely transparent to completely opaque. As a consequence, some image pixels at a fixed retinal location were rendered invisible no matter where the eye was pointing on the monitor, simulating a lesion on the retina. The quality of the gaze-contingent display depends on the eye tracker sampling rate, monitor frame rate, data communication delay between the host and display computers, and the image manipulation speed of the display computer. Cornelissen et al. [30] used an earlier Eyelink I to create gaze contingent display and reported that the length of the entire system's delay (from the completion of a saccade to the image update) was ≤ 20 ms. The Eyelink II system used for this experiment had twice the sampling rate (500 vs. 250 Hz) and much more modern host and display computers. An estimate of the average redrawing time of the search stimulus with the simulated scotoma was ≤ 5 ms. This delay is subjectively insignificant, and none of the subjects in the study reported any perceived delays between the simulated scotoma and their eye movements.

2.3 General Methods and Procedures

Before each simulated scotoma search session (block of trials), the headband of the eye tracker was positioned on the subject's head. Subjects were then situated in a chin rest and the position and focus of the eye cameras on the headband were independently adjusted to establish reliable tracking over the search area, as indicated by the manufacturer's camera setting routine. Next, a set of calibration and validation procedures was conducted, in which a stimulus dot randomly jumped to 9 designated calibration locations on the monitor and stayed there for 1000 ms. The subject was asked to follow the dot with his/her eyes. The procedures were successful when a set of built-in criteria for spatial accuracy and repeatability were met. Accuracy varied slightly across calibrations, but an acceptable calibration gave a foveal position accuracy that was generally less than 0.2° in the vertical and horizontal directions. Each trial in a session started with a drift correction in which a stimulus dot was shown at the center of the monitor and stayed there. The subject was asked to fixate the dot before pressing a key on the computer keyboard. The correction was successful if the fixation was stable and the average fixation was used to correct shifts of the calibration grid caused by small changes in head position or slip of the headband in the previous trial. The drift correction ensured that every trial started with the fovea at the center of the screen. Then the search stimulus and a simulated scotoma were shown and the subject started to search with the scotoma in place. Different auditory tones were used to signal correct and incorrect responses, and these occurred immediately when a response was given.

2.3.1 Stimulus description, visual search task and general procedure

Typically, feature search stimuli are presented in a uniform rectilinear grid spread over a given area of the visual field, the search area, and are presented until the subject responds. Figure 1 shows an example of a 9 x 9 grid with 81 possible grid locations where target and distractors can be presented. In the example the target is black and several light grey distractors are spread over a search area of 10°. A square search area of F° x F° is covered by a square M-row by M-column search grid giving a total of M x M grid locations. Grid size determines the spatial resolution of the search test and the smallest scotoma it can detect. The search items, the target, and the distractors, referred to as the stimulus array, were always centered on grid locations. In each search session, the number of search items, N, was fixed and N was the set size of the session. Because N was always smaller than M x M in our experiments, not all grid locations were occupied by search items in any trial. Each search session was made of M x M positive trials, trials that had 1 target and N-1 distractors, so that the target was displayed on every grid location once in random order. Once the target location in the search grid was determined in a trial, the locations of the distractors were randomly selected from the remainder of the grid locations. Each search session also contained 25% negative trials, trials that had N distractors, and no target. The locations of the N distractors were randomly selected from the M x M grid locations.

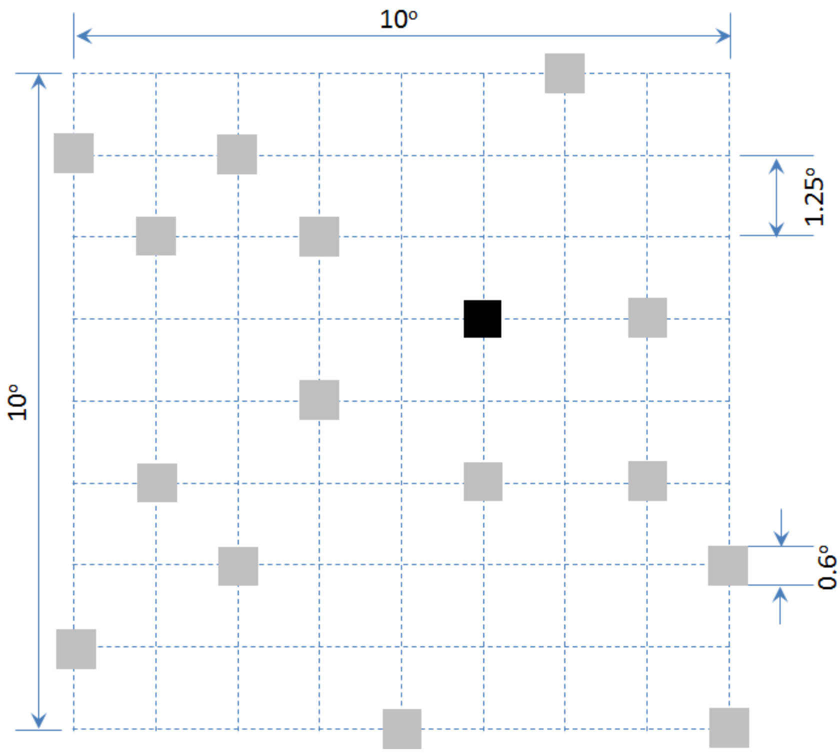


Figure 1: An example of a feature search grid, the search stimuli, and stimulus array. The example is taken from experiment 1 and shows a 9x9 grid covering a 10° x 10° search area, with a mean horizontal and vertical separation of 1.25° between rows and columns. The target and distractors were 0.6° x 0.6° squares, differing only in contrast. The example shows a positive trial with a set size of 16; one target and 15 distractors. The dotted lines are drawn to show the underlying search grid and were not present in the real test

The placement of a simulated scotoma was relative to a grid location, more specifically, relative to the grid location occupied by the target in a positive trial. This placement defined the relative position between the scotoma and the target at the beginning of each trial. It was ensured by the drift correction procedure at the beginning of each trial and was no longer valid once the subject moved his/her eye. If the scotoma was coincident with the target, the scotoma was centered at the grid location of the target as illustrated in Figure 2a. If the scotoma was larger in size than the target, the scotoma would completely conceal the target. If the scotoma was adjacent to the target, as illustrated in Figure 2b, the scotoma was centered at the center of one of the four grid squares adjacent to the grid location occupied by the target (the grid reference location). The actual scotoma location for a search session was randomly selected from the 4 possible adjacent locations, unless the target was on the borders of the search grid, in which case, the scotoma was always placed in the interior side of the grid. Depending on the sizes of the target and the scotoma, a scotoma on an adjacent location may conceal none of, part of, or the entire target.

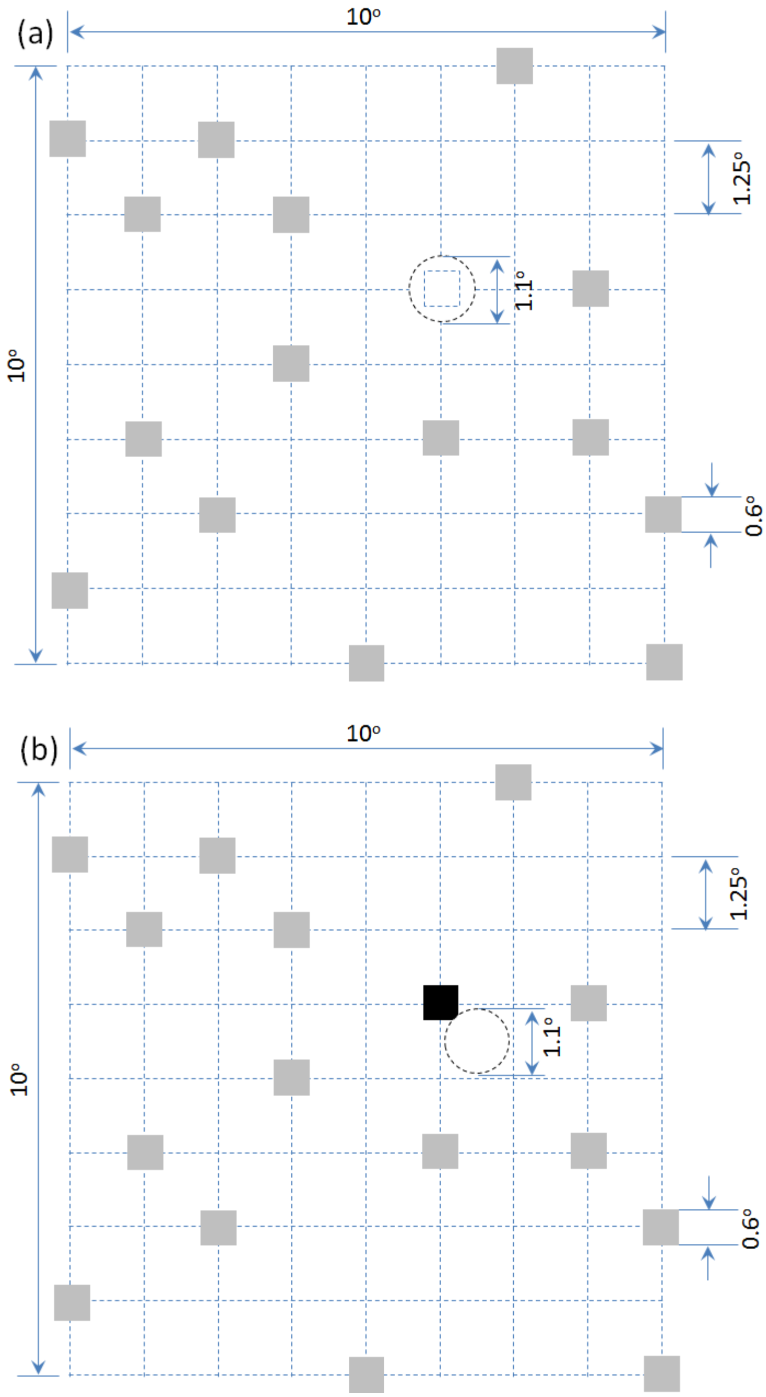


Figure 2: Example of the initial positions of the target and a 1.1° simulated scotoma taken from experiment 1. The simulated scotoma is delineated by a dashed circle to show its location and size in the graph. The circle was not shown with the real stimulus. (a) Scotoma coincident condition. The dashed square indicates the target coincident with and therefore under the simulated scotoma, and thus it can't be seen. (b) Scotoma adjacent condition. The target is located adjacent to the target and obscures a small part of it

Scotoma were circular in shape but the edges were blurred using a Gaussian filter with a standard deviation (σ) set at 10% of the scotoma diameter (e.g., σ = 0.06 for the 0.6° scotoma). What this means is that the effective size of the scotoma was slightly larger than the defined size. Figure 3 shows the transparency profile of a simulated scotoma and the effect of the scotoma partially obscuring a search item (a black square). The mask transparency changes gradually from opaque to completely transparent outside of the defined scotoma diameter, allowing the search item to be seen in its full contrast to completely opaque inside the scotoma, rendering part of the search item invisible.

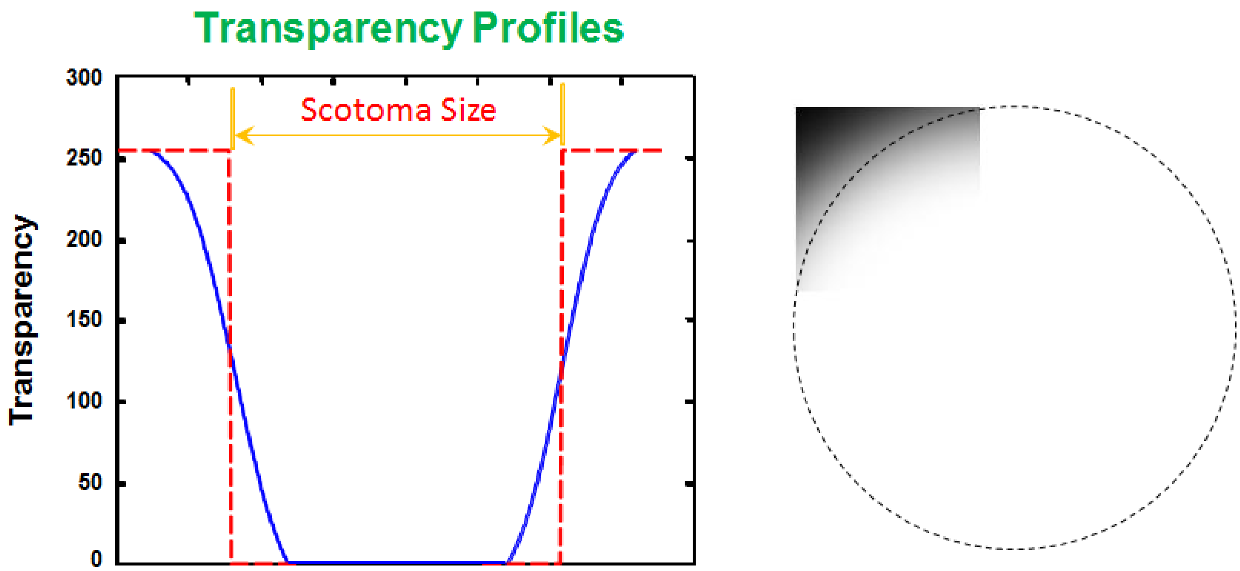


Figure 3: Illustration of the scotoma profile (left) and how it potentially interacts with a search item that is positioned adjacent to the center of the scotoma

The primary feature of interest in experiment 1 was achromatic contrast. The target and distractors were presented on a white background with a luminance of 65 cd/m^2. The target was dark grey (6 cd/m^2) and the distractors a light grey (17.4 cd/m^2) which yielded contrasts of 83% and 58%, respectively. Limited testing with chromatic targets and distractors was also completed in experiment 1. For the color feature, there were two color conditions. In one the target was red and the distractors were green; in the other, the target was blue and the distractors were yellow. The chromatic targets and distractors were approximately luminance matched in order to bias detection to favor chromatic mechanisms. As expected from the pilot data, the chromatic results of experiment 1 closely paralleled the achromatic ones and to simplify the presentation, color condition results are not shown. The achromatic contrast feature was exclusively used in experiment 2.

The contrast feature yielded a very salient stimulus where the target popped out from the distractors as soon as the stimulus array was presented. The subjects' task was to indicate as quickly as possible if the target was present or if no target was present. A typical feature search experiment consisted of a set of "positive" trials over which the target was eventually presented at each location of the search grid and a set of "negative" trials where no target was presented, only distractors. The negative trials serve to ensure the subject is paying attention to the task and not simply reporting the presence of the target as soon as the stimulus array is presented.

In low vision patients with small scotoma outside the fovea, if the target of a positive trial is imaged in or near the scotoma, it can be concealed or distorted by the scotoma and does not pop out from the background of distractors. Therefore, to these patients, a positive trial can be perceptually similar to a negative trial when the target is imaged in or near the scotoma. Since normal as well as low vision patients take significantly more time to make a "target absent" response to a negative trial than a "target present" response to a positive trial, a significantly longer reaction time to a positive trial may indicate the presence of a scotoma at or near the location of the target.[22] It is also possible that a patient may make a "target absent" response without making an effort to ensure no target is present. This will result in a "miss" error. Therefore, each positive trial of the search test is an independent evaluation of the functional integrity at the location of the target, and the presence of a scotoma can be signified by a long RT or a miss error.

Based on lesion sizes from laser therapy studies, [25, 26] the overall goal of the study was to determine if it was possible to detect a 1.1° scotoma in the central 10° or 20° of the visual field using the feature search paradigm. The theoretical capability of a feature search test in detecting a scotoma is determined by the search area, search grid size, and search item size. If a M x M square search grid is used to detect a scotoma on a F° x F° square field, the separation between adjacent grid points in horizontal and vertical direction is $S = F / (M-1)$ degrees. If the search items are T° x T° squares, then a scotoma with a maximum dimension of $(S – T)$ degree may not be detected because it can fit between two adjacent testing locations without touching the search target. For example, in Figure 1, where a 9 x 9 grid is used to survey a 10° x 10° field, the separation between adjacent grid points is S = 10 / (9-1) = 1.25°. The search items are 0.6° x 0.6° squares. This search stimulus may not be able to detect a scotoma 1.25° – 0.6° = 0.65° or smaller. In practice, however, the subject's eye is constantly moving, even during fixation. Therefore, the scotoma may not always sit in the gap between two adjacent testing locations. Also, the amount of spatial overlap between the search target and the scotoma needed to significantly reduce the salience of the target is unknown. Therefore, the size of the scotoma that can be detected by a given search stimulus is an empirical question.

2.3.2 Statistical Analysis

Each search session results in four types of responses and corresponding response times. A Hit response is a correct report of the presence of a target in a positive trial. A Miss response is a wrong report of the absence of a target in a positive trial. A Correct Rejection (CR) is a correct report of the absence of a target in a negative trial. A False Alarm is an incorrect report of the presence of a target in a negative trial. Because the total numbers of positive and negative trials in each search session were fixed and known, only two of four response rates were independent.

Eye movement data included number of saccades made on each trial, saccade amplitude and speed, the number of fixations, and fixation duration. Data on the number of saccades and fixations made were analyzed for experiment 1. Those results closely paralleled the RT for Hits (RTHit) data and a similar analysis was not conducted for experiment 2. The focus of the analysis was on the RTHit as this was the metric that would most likely be used in a screening test. Hit and False Alarm rates were also examined to determine the subject's accuracy in performing the search task. Individual miss trials may be associated with the presence of a scotoma near the target location. Standard and repeated measures analysis of variance (ANOVA) and dependent t-tests were used (SPSS version 20).

2.4 Experiment 1

2.4.1 Experiment 1 Methods.

2.4.1.1 General.

Parameters of the feature stimulus have direct impacts on its effectiveness and efficiency in small scotoma detection. Finer search grids and large search item sizes increase the chance of detecting smaller scotoma, but also increase the number of trials of the test. Experiment 1 used several combinations of search area, grid size, and target size to study the detectability of simulated scotoma of different, but known, sizes. In experiment 1 a simulated scotoma was always paired with a target. Scotoma size and the position of the scotoma relative to the target (coincident with or adjacent to) were varied. Since target locations varied randomly trial by trial, so did the scotoma location in the search area, although position, coincident with or adjacent to the target was fixed during a search session. Experiment 1 was designed to determine what parameters should be used in experiment 2. The feature of primary focus was achromatic contrast. Several pilot experiments indicated the range of scotoma sizes to be tested as well as grid sizes and item sizes (targets and s). The pilot experiments also provided guidance on the item density to use and the visual feature to focus on; color or achromatic contrast. As noted previously, limited data with color as the feature was collected, but are not shown because they yielded the same results as the contrast feature.

2.4.1.2 Stimulus Parameters and Test Conditions.

Scotoma detection was tested for two square visual search areas, 10° and 20°. For the 10° area, two grid sizes were used, 9 x 9 and 11 x 11, corresponding to 1.25° and 1.0° minimal spatial separation between adjacent search items. Target and distractors were 0.6° and 0.5° squares for the 9 x 9 and 11 x 11 grids, respectively. The size difference allowed approximately the same spacing between items in the two grids. The number of items presented on each trial was set at 20% of the total number of grid locations. Thus, for the 9 x 9 grid, sixteen items, and for the 11 x 11 grid, twenty four items were presented on each trial. Target and contrasts for the achromatic contrast feature were 83% and 58%, respectively. Twenty-five percent (25%) of trials were negative and contained no target. Since the target was presented at all locations in the grid, this meant a total of 101 (81 positive and 20 negative) and 151 (121 positive and 30 negative) trials in a search session for the smaller and larger grids, respectively.

Three scotoma sizes were tested: 0.6°, 1.1°, and 1.6° in diameter. Three scotoma conditions were tested: no scotoma, which served as the baseline, scotoma centered on the grid location occupied by the target, and scotoma located 45° adjacent to and centered at the center of one of the four grid squares adjacent to the grid location occupied by the target. The scotoma arrangements were depicted in Figures 1 and 2. In Figure 1 no scotoma was present. Figure 2a shows the scotoma coincident with and covering the target and in Figure 2b the scotoma was located adjacent to the target. Positive trials were randomly dispersed within a search session as were target and locations. In summary, the 10° search area condition was a 2 grid size x 3 scotoma size x 3 scotoma arrangements (includes no scotoma) experimental design. For the 20° search area, grid sizes were 11 x 11 and 13 x 13 and target and sizes were 1.0° and 0.8° on a side, respectively. Scotoma sizes, locations, and percentages of total items presented on target and no target trials were the same as for the 10° search area. Similarly, the 20° search area condition was a 2 grid size x 3 scotoma size x 3 scotoma arrangement design.

Data collected included RTHit and RT for correct rejections (RTCR) as well as the proportion of hits and correct rejections. Eye movement data included number of saccades made on each trial, saccade amplitude and speed, the number of fixations, and fixation duration. It is important to note that the geometric relationship between a scotoma and the target is valid only at the beginning of a scotoma present trial, which is guaranteed by the drift correction at the beginning of each trial. Once the trial starts and the eyes may move, the geometric relationship between a scotoma and the target may not be valid. An eye movement made by the subject moves the scotoma but not the search stimuli and will reveal the initially concealed target so that a correct response can be made. This is the reason a gaze-contingent display is used to simulate a retinal lesion, otherwise, one could just display a stimulus array with a hole in it, but that does not simulate the effects of a real scotoma that moves with the eye.

Within each search session, the target appeared once at all locations on the grid. In the search sessions of experiment 1, a scotoma was present every time a target was present, which means that at each target present trial; there was a small scotoma at a different retinal location. No scotoma was present on target absent trials. This differed from the case of a real scotoma which would be fixed at one location on the retina and always present. However, pairing a scotoma with a target on each target present trial was a more efficient way to collect a large amount of information about the effects of grid size, scotoma size, and location on target detection. Because each search trial had randomized target position and composition, each trial with a simulated scotoma in a search session could be considered an independent assessment of a particular scotoma.

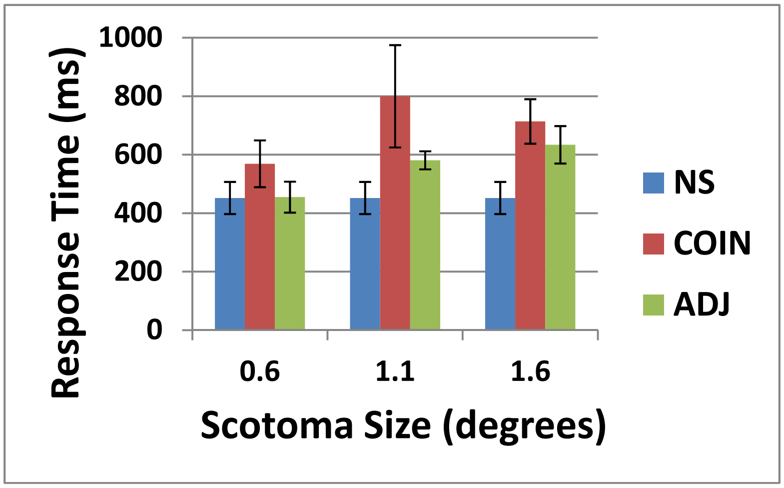
2.4.1.3 Procedure.

Testing took place over ten, 1 hour test sessions. Multiple search sessions with and without a simulated scotoma were completed within each 1 hour visit. The 10° search area data were collected first. During the first test session subjects were familiarized with the task and given practice on it. Prior to practice, subjects were shown an example of the search stimuli with a target present. The target was dark grey and the distractors were light gray. Subjects were told that a trial consisted of presentation of a set of distractors and that on some trials a target would also be present, as in the example, but on some trials no target would be present. They were told that the locations of the distractors and target, if present, would vary on each trial and that their task, when the stimulus array appeared, was to respond as quickly as possible with an appropriate button press that the target was present or absent. They were shown which buttons to press on the five key response box for each response type. They were also instructed that they would initiate each trial by first fixating on a central fixation point and then pressing the center button on the response box (two buttons were not used and were inactive). They were informed that if fixation was not stable or accurate that the stimulus array would not be presented when the center button was pressed and to re-fixate and try again. If fixation was accurate the fixation target would disappear and be immediately replaced with the search stimuli. After instruction, subjects were positioned in the chin rest, the cameras were set, and the calibration routine completed as previously described. After calibration, a set of 50-60 practice trials was completed with a 9 x 9 grid size on the 10° search area. No scotoma was present and contrast was the target feature. This situation presented them with a standard feature search task. After the familiarization trials, subjects were asked if they felt they understood the task and were comfortable with the response keypad. All subjects responded affirmatively. Subjects then completed a set of three no scotoma (baseline) search sessions for the 9 x 9 grid size on the 10° search area. Each session consisted of 97 trials. At the end of practice, subjects had completed approximately 350 trials. No time limit to make a response was imposed, but subjects were not informed about this. Since subjects initiated each trial, they controlled the pace of the experiment.

2.4.2 Experiment 1 Results.

2.4.2.1 Ten Degree Search Area.

The RTHit results for the 10° search area are summarized in Figure 4. Repeated measures ANOVA for the 9 x 9 grid (Figure 5, top panel) indicated significant main effects of scotoma size ($F = 20.06$, $p = 0.003$) and position ($F = 43.92$, $p = 0.001$). The interaction of size and position was also significant ($F = 11.46$, $p = 0.007$). Post-hoc analysis indicated that compared to the no scotoma condition (baseline), average RTHit was significantly longer for all scotoma sizes when the scotoma were coincident with the target. In contrast, RTHit for the scotoma adjacent condition was significantly elevated for the 1.1° and 1.6° scotoma sizes but not for the 0.6° size. Results for the 11 x 11 grid size (Figure 4, bottom panel) were similar. There were significant main effects of scotoma size ($F = 16.74$, $p = 0.009$) and position ($F = 23.31$, $p = 0.002$) and a significant interaction effect ($F = 9.34$, $p = 0.023$). Average RTHit for the scotoma coincident condition were significantly longer than baseline for all scotoma sizes (t-test range -4.9 to -8.0, $p = 0.008$ to 0.001) and RTHit for the scotoma adjacent conditions were significantly elevated for the 1.1° ($t = -4.4$, $p = 0.012$) and 1.6° ($t = - 8.0$, $p = 0.001$) scotoma sizes but not for the 0.6° size.



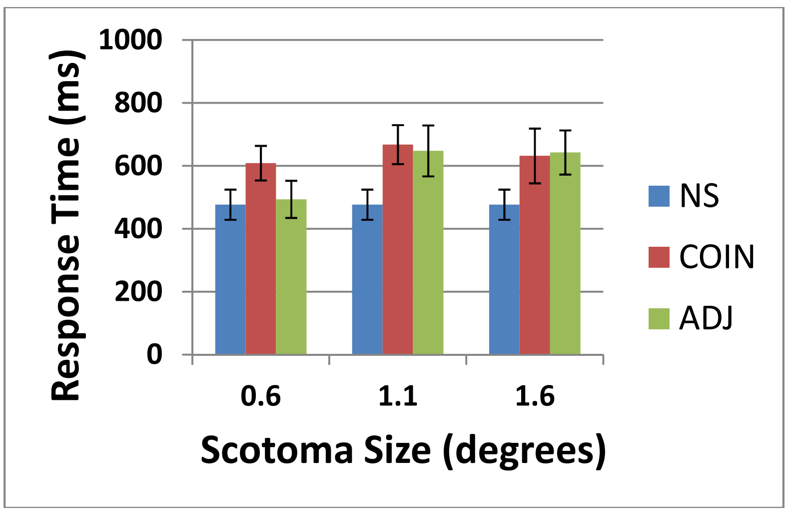


Figure 4: Average response times (milliseconds) for hits (RTHit) for the 10° search area and 9 x 9 grid (top panel) and 11 x 11 grid (bottom panel) as a function of scotoma size and position (no scotoma (NS), coincident with (COIN) or adjacent to (ADJ) a grid location)

Hit and correct rejection rates and response times for correct rejections (RTCR) were also tracked. Hit rates were high regardless of scotoma condition averaging slightly over 98% for the group collapsed over all test conditions. Even for scotoma coincident condition where the target was completely obscured, hit rates did not change. In other words, subjects rarely reported that a target was not present when one was (a miss) and responded with a high degree of accuracy. Similarly CR rates were also high, averaging 95% for the group over all conditions. In other words, subjects rarely reported a target present when one was not (false alarm). Although CR rates across subjects showed more variability, with two subjects having rates of 90% while the remaining three subjects had rates over 97%, like hit rates, the CR rates did not depend on the scotoma condition. As is typical of feature search, RTCR was longer than RTHit and averaged 961 ms for the group, again collapsed over all conditions, compared to 559 ms for RTHit. RTHit showed more variability as expected given the differences between the scotoma conditions as shown in Figures 1 and 2; however, even in the scotoma coincident condition the average RTCR was higher than the average RTHit for that condition.

Several eye movement parameters (number of saccades and fixations per trial) were analyzed globally to determine if further analysis was warranted. The results for the number of saccades made for the 10° search area and the two grid sizes are shown in Figure 5. Comparing the saccade results with the RTHit results in Figure 4, it can be seen that they follow similar patterns. Test conditions that generated longer RTHit also generated more saccadic eye movements. The strength of this association between RTHit and number of saccades is illustrated in Figure 6 for the 9 x 9 grid, 10° search area where RTHit is plotted as a function of the number of saccades. As RTHit increased, so did the number of saccades; the relationship was strong, as evidenced by a correlation coefficient ($r = 0.86$). Similar results were found for the 11 x 11 grid size ($r = 0.68$).

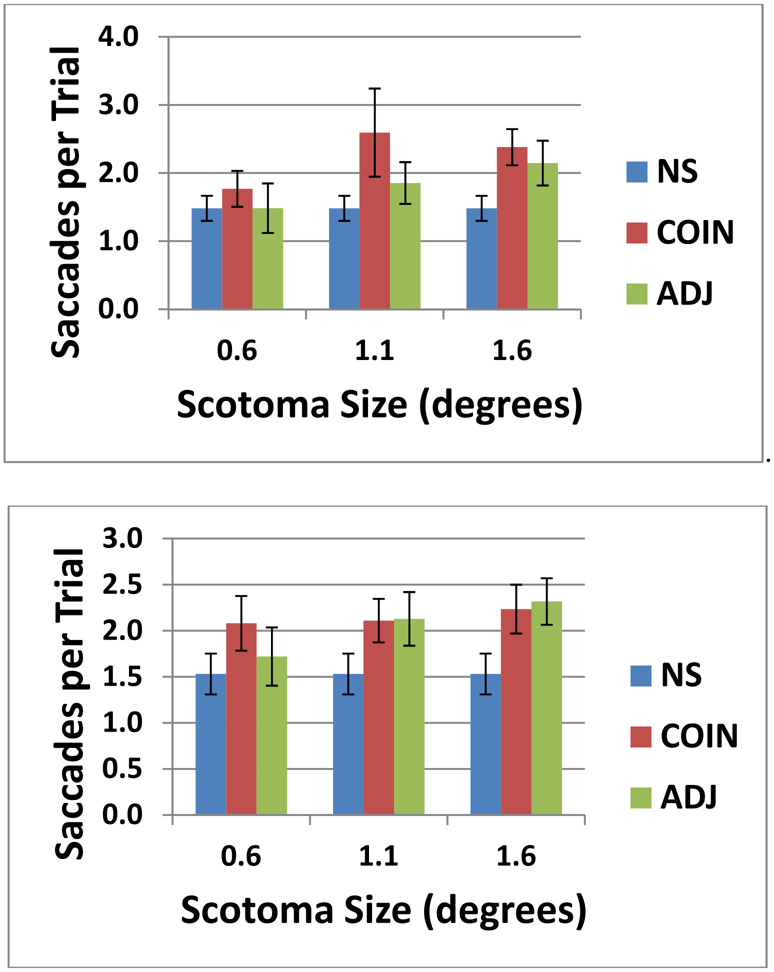


Figure 5: Average saccadic eye movements made per trial for the 10° search area with the 9 x 9 (top panel) and 11 x 11 (bottom panel) girds as a function of scotoma size and position (no scotoma (NS), coincident with (COIN) or adjacent to (ADJ) a grid location)

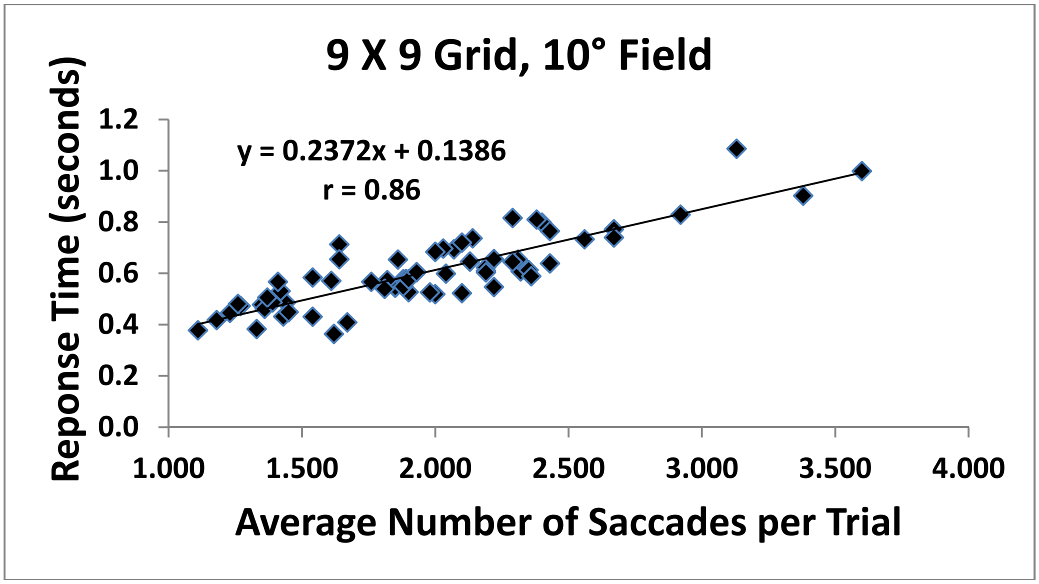


Figure 6: Scatterplot of the RTHit as a function of average number of saccades per trial. Regression line is a linear fit to the data

2.4.2.2 Twenty Degree Search Area Results.

The RTHit results for the 20° search area are summarized in Figure 7. For the 11 x 11 grid (Figure 7, top panel), repeated measures ANOVA indicated significant main effects of scotoma size ($F = 15.40$, $p = 0.006$) and position ($F = 11.69$, $p = 0.024$). The interaction of scotoma size and position was also significant ($F = 15.81$, $p = 0.003$). Post-hoc analysis indicated that, for the scotoma coincident conditions, RTHit was significantly longer than baseline for the 1.1° ($t = -4.48$, $p = 0.011$) and 1.6° ($t = -3.17$, $p = 0.034$) scotoma sizes but not the 0.6° size. For the scotoma adjacent condition, none of average RTHit averages for any scotoma size were different from the no scotoma condition. For the 13 x 13 grid size (Figure 7, bottom panel) there were significant main effects of scotoma size ($F = 35.68$, $p = 0.003$) and position ($F = 71.64$, $p < 0.001$) and a significant interaction effect ($F = 10.52$, $p = 0.017$). Average RTHit for the scotoma coincident condition was significantly longer than baseline for the 1.1° ($t = -9.5$, $p = 0.001$) and 1.6° ($t = -5.5$, $p = 0.005$) but not for the 0.6° size. For the scotoma adjacent condition, only the average RTHit for the 1.6° scotoma size was significantly longer than baseline ($t = -7.4$, $p = 0.002$).

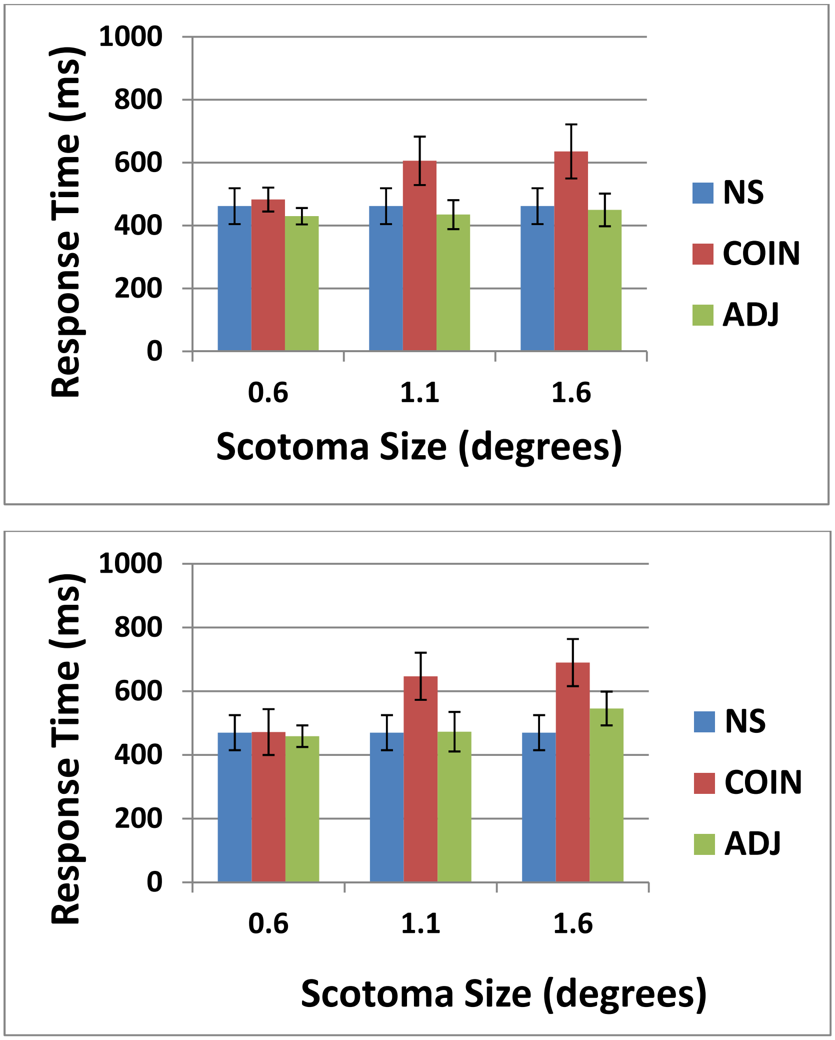
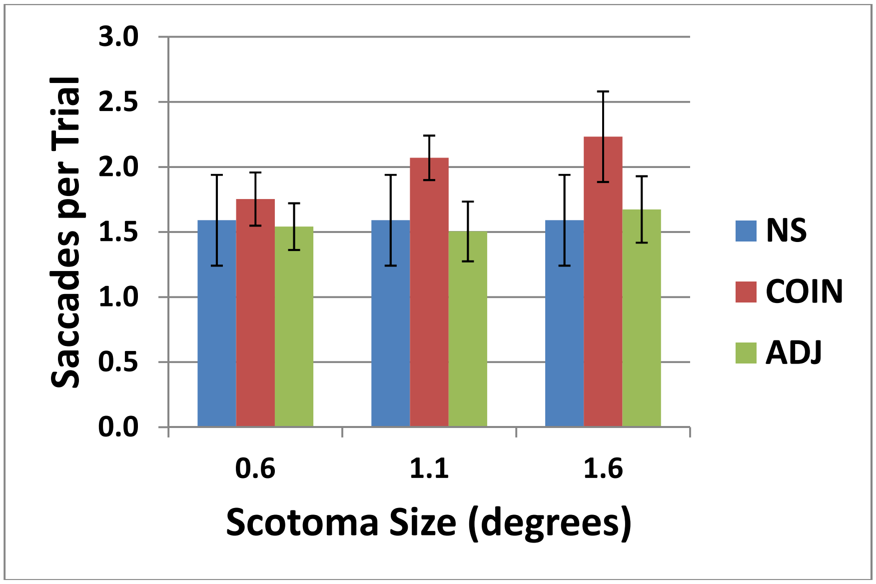


Figure 7: Average response times for hits (RTHit) for the 20° search area with the 11 x 11 (top panel) and 13 x 13 (bottom panel) grids as a function of scotoma size and position (no scotoma (NS), coincident with (COIN) or adjacent to (ADJ) a grid location)

The results for the number of saccades made for the 20° search area and two grid sizes are shown in Figure 8. As for the 10° search area, the number of saccades made in the different scotoma conditions follows the pattern of RTHit. Test conditions that generated longer RTHit also generated more saccadic eye movements. The correlations between number of saccades and RTHit for the 11 x 11 and 13 x 13 grids were strong as indicated by r values of 0.72 and 0.81, respectively. The strong association between response times and number of saccades suggests the two types of measure are conveying similar information. The results also support the hypothesis that when the target is obscured by a scotoma, either partially or totally, that subjects begin making additional eye movements in order to uncover it and reveal its presence before responding.



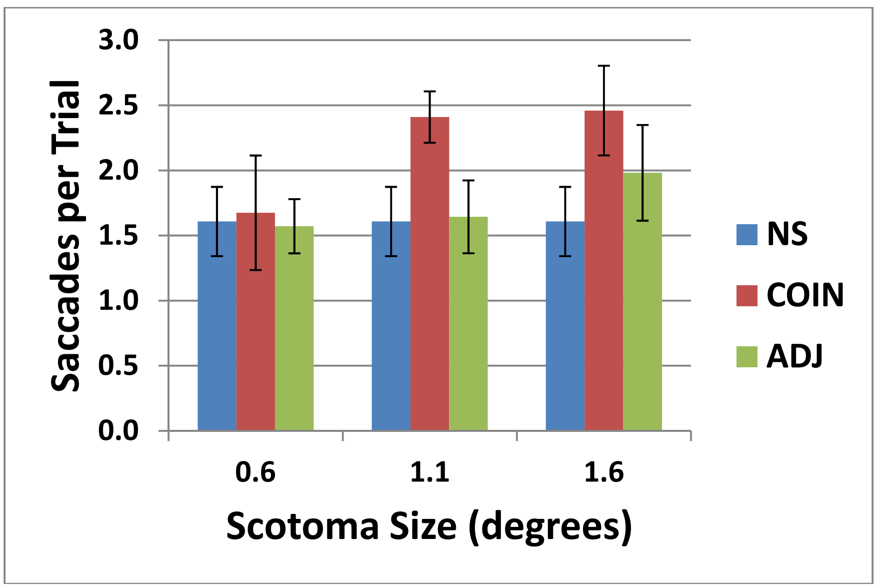


Figure 8: Average response saccadic eye movements made for the 20° search area with the 11 x 11 (top panel) and 13 x 13 (bottom panel) grids as a function of scotoma size and position. No scotoma (NS) saccade data are plotted for comparison

2.5 Experiment 2

2.5.1 Experiment 2 Methods

2.5.1.1 Overview.

Experiment 2 was designed to determine if the visual feature search paradigm could be used to detect small retinal lesions at fixed locations. Search area, grid size, search item size, and scotoma size were set based on experiment 1. Unlike experiment 1, scotoma position in experiment 2 was always adjacent to a specific grid location and the scotoma was present throughout an entire search session. Scotoma size was varied as was search area. However, for each search area only a single grid size was used.

Only the scotoma adjacent condition and a control were tested. The scotoma adjacent condition represents the partial occlusion condition, which is probabilistically more likely to happen than the complete occlusion condition (scotoma coincident) because targets imaged within a band around the scotoma can all be partially occluded while only targets that all fit in the scotoma can be completely occluded. The scotoma coincident is the best case condition and in experiment 1 consistently resulted in elevated RT except when the scotoma were smaller than the target. Another condition that was not tested was to have the scotoma located between two horizontal or vertical item locations. This would be expected to yield intermediate results given the closer spacing of items relative to the scotoma, but time constraints did not permit it to be tested.

2.5.1.2 Stimulus Parameters and Test Conditions.

Scotoma detection was tested for two square search areas of 10° and 20°. For the 10° area, the grid size was 11 x 11, item size was 0.5°, scotoma sizes were 1.1° and 1.6°, and scotoma were positioned adjacent to grid locations 13 (column 2, row 2), 59 (column 6, row 4) or 81 (column 8, row 4). In terms of eccentricity, the target locations were at 5.65°, 2°, and 2.83° from fixation at the fovea. Grid locations are numbered beginning in the upper left corner of the grid, down a column, and then back to the top of the next column, and so on. Figure 9 illustrates the grid locations (black squares) for the 11 x 11 grid to which scotoma locations were referenced for the 10° search area. For illustration, the grid locations are completely filled with items, although in practice only 20% of the grid locations would have items in them on a given trial.

The set of grid reference locations was slightly different for the 20° search area, with the grid location directly above the grid center for the 10° search area moved to near the bottom of the grid. The other two grid locations were similar relative to those of the 10° search area (upper left corner and halfway between fixation and the upper right corner). For the 20° search area, the grid size was 13 x 13, item size was 0.8^{o}, scotoma sizes were 1.6° and 2.2°, and scotoma were adjacent to grid locations 29 (column 3, row 3), 89 (column 7, row 11), and 108 (column 9, row 4). In terms of absolute eccentricity, these grid locations were at 9.43°, 6.67°, and 6.01° from fixation at the fovea, respectively. For each search area, the design was a 1 grid size x 2 scotoma sizes x scotoma arrangement (adjacent) x 3 grid (target) locations (eccentricity). A no scotoma baseline condition was also completed. Each condition was repeated 3 times for a total of 18 scotoma and 3 baseline search sessions per search area size.

The number of items for both grid sizes was set at 20% of the total number of items that could be presented. For the 11 x 11 and 13 x 13 grids 24 and 34 items were presented on each trial, respectively. Twenty-five percent (25%) of trials were negative and contained no target. Since the target was presented once at all locations in the grids, together with the negative trials this meant a total of 151 (121 positive) and 211 (169 positive) trials in a search session for the smaller and larger grid sizes, respectively. Scotoma was circular in shape, but the edges were blurred using a Gaussian filter with a standard deviation set at 10% of the scotoma diameter.

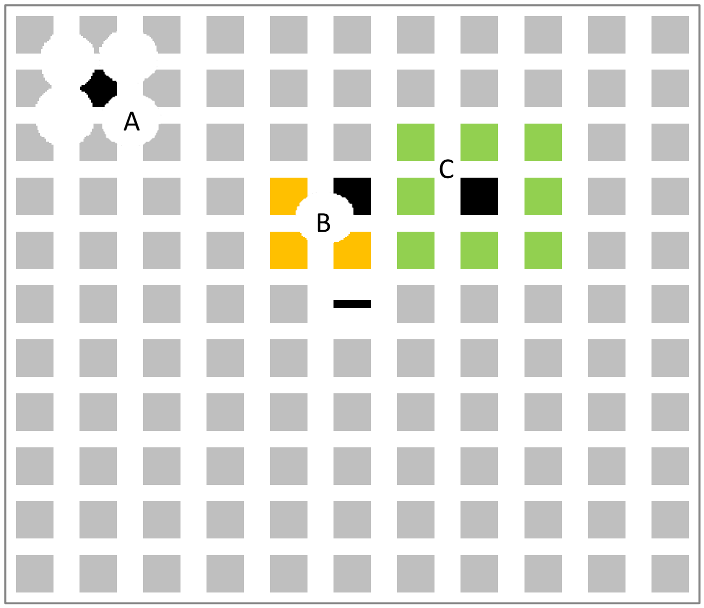


Figure 9: The three grid locations (black squares) for the 11 x 11 grid on the 10° search area used as the references for scotoma placement. The black squares are centered at grid locations 13, 59, and 81. A: Illustration of the four possible positions where scotoma could be placed relative to a grid reference location (black square). Only one of the four was used during a search session, but any of the four could be used in different search sessions; B: Illustration of other grid locations (orange squares) in addition to the reference grid location that will be also be adjacent to the scotoma during a search session; C: Illustration of all grid locations besides the grid reference that could be affected in multiple search sessions where across search sessions scotoma position can vary relative to the grid reference

2.5.1.3 Procedure.

The basic procedure was essentially the same as for experiment 1. Prior to testing, subjects were given instructions, familiarized with the task, and given practice as described for experiment 1. As in experiment 1, fixation on the central fixation target was required before a trial could start. The subjects' task was also the same: to indicate as quickly as possible with button presses if a target was present or if it was not. Testing for the 10° search area was completed first.

2.5.1.4 Data Analysis Overview.

As previously described, three different specific grid locations to which the scotoma were referenced were tested for the 10° and 20° search areas. These reference grid locations varied in eccentricity and orientation in the search area as illustrated in Figure 9, for the 10° search area, by the black symbols. The method for testing was set up so that scotoma position was fixed relative to a grid reference location within a search session but randomly assigned between each session to the center of one of the four grid squares adjacent to a grid reference location. Figure 9A shows the four possible places relative to a grid reference location where a scotoma could be assigned. As noted, once a scotoma position was assigned for a search session it was fixed for the entire session and the scotoma was present on each trial in that session. Thus, as illustrated in Figure 9B, during a single search session, there were four grid locations that surrounded the scotoma and a target presented on any of them could potentially fall under the scotoma and be obscured, either completely or partially depending on scotoma size. However, with three search sessions completed per subject for each reference grid locations, it was highly probable that across the three search sessions and the nine subjects, the scotoma would be placed at more than one location out of the four possible. This effectively expands the number of grid locations where a target and scotoma could interact when the results are averaged. Figure 9C shows an example of the nine grid locations surrounding a reference location where targets appearing at those locations, plus the grid reference, could potentially be influenced by the presence of a scotoma. We note this as some of the RTHit maps shown later will illustrate, scotoma position randomization and averaging over multiple search sessions effectively increased scotoma size and often resulted in average RTHit maps with rather broad domes of elevated response times. Single search session data were also examined since, during a single search session, scotoma position was fixed and fewer grid locations (4) where a target appeared could potentially be affected by the presence of a scotoma. However for statistical analysis, we focused on RTHit for the grid reference location since across multiple search sessions it was the one location where a target presented on it was always adjacent to the scotoma.

RTHit results for each search area were treated separately and two methods were used to analyze it. In the first method, for each subject the three search session RTHit results for each grid reference location (Targ) and scotoma size condition were averaged and compared to the average RTHit for a symmetrical grid location in the opposite hemifield. The symmetrical grid locations are referred to as comparison (Comp) locations. In the second method, we compared RTHit for the reference grid location (Targ) with the average RTHit (Avg) from all of the grid locations in a condition.

In addition, RTHit maps were generated for each test condition in experiment 2. An example of a map is shown in Figure 10. The maps are 3D plots of RTHit as a function of item location in the grid. The maps are primarily useful for qualitative comparison. For each subject and condition this consisted of averaging the matrix of RTHit for the three search sessions. For example, for the 10° search area there were 3 grid locations to which scotoma were referenced and 2 scotoma sizes plus a no scotoma condition, thus seven RT maps were generated for each subject. The same number of maps was created for the 20° search area for a total of 14 maps per subject. The no scotoma maps were not used in any analysis and generally were rather flat. Figure 10 shows the average 10° search area no scotoma RT map for the nine subjects for illustration. The map is rotated and tilted downward slightly to give a view of looking down on the map. Response times ranged from 348 to 508 ms (median = 395 ms); even though the map is not completely flat, there was no strong trend suggesting RT increased as eccentricity increased.

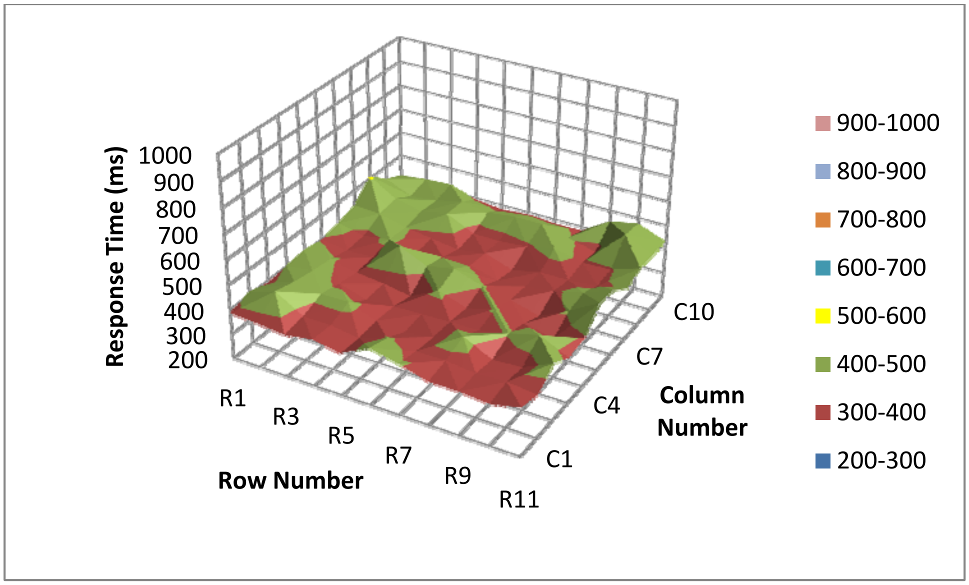


Figure 10: Average RTHit for the 10° search area for the no scotoma condition as a function of column and row positions. Grid size was 11 x 11

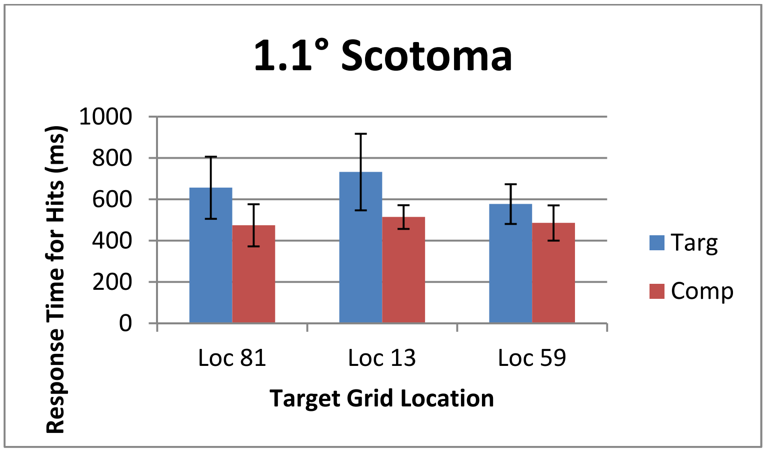
2.5.2 Experiment 2 Results

2.5.2.1 Ten Degree Search Area.

Table 1 lists the group average RTHit values and standard deviations for the different comparison methods and test conditions. Figure 11 illustrates RTHit results for one of the sets of three comparisons listed Table 1 and shows the differences between RTHit values measured at the reference target location Targ versus the Comp location. Results for the other method are not shown because of similarity. As Figure 11 shows, for both scotoma sizes and at all scotoma locations, RTHit averages for the target locations (Targ) are longer than for the comparison locations. For the 1.1° scotoma size, the average RTHit difference was 145 ms. For the 1.6° scotoma it was 265 ms. The greater difference for the larger scotoma is due to generally longer RTHit Targ, with an average of 745 ms, compared with 656 ms for the 1.1° scotoma, while RTHit for the Comp locations for both scotoma sizes are nearly the same.

Table 1: Ten degree search area average RTHit values for the different scotoma sizes and reference locations for each of the response metrics

Scotoma size/grid location	Targ	Comp	Avg
	RTHit (sd)	RTHit (sd)	RTHit (sd)
1.1/81	657 (150)	475 (102)	529 (117)
1.1/13	732 (185)	515 (57)	507 (92)
1.1/59	578 (96)	486 (85)	495 (65)
1.6/81	812 (237)	451 (83)	496 (59)
1.6/13	744 (162)	467 (81)	458 (31)
1.6/59	676 (176)	428 (92)	481 (57)



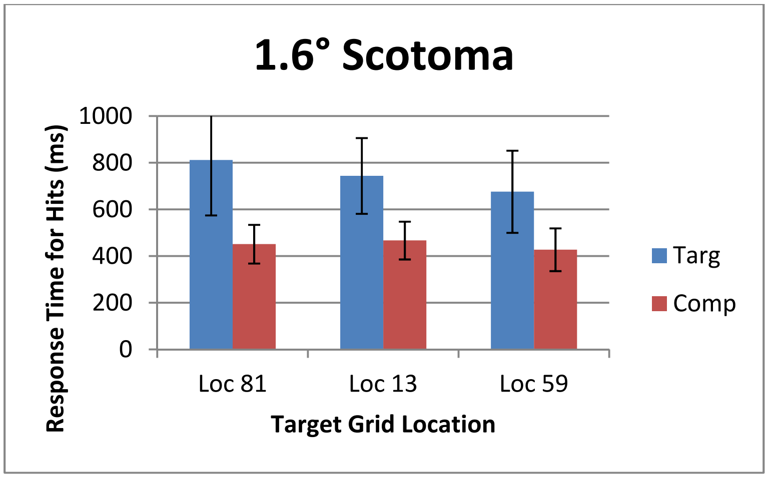


Figure 11: Ten degree search area, three trial average RTHit for the reference location (Targ), and a comparable (Comp) location in the opposite hemifield as a function of reference grid location for the two scotoma sizes. Error bars ± 1 sd

Both methods of analysis of the RTHit data produced similar results. Repeated measures ANOVA findings are listed in Table 2. For both methods, there was a significant effect for the type of RTHit metric: Targ versus Comp and Targ versus Avg. There were no significant main effects for scotoma location or scotoma size. The lack of a scotoma size effect is likely due to the fact that the analysis involves RTHit data for the grid locations where no scotoma were present and for which RTHit values were very similar across scotoma sizes and grid reference locations. However, the interaction between metric type and scotoma size was significant for the Targ versus Avg comparison and trended towards significance for the other. This indicates that differences in RTHit between metrics were influenced by scotoma size, with the larger scotoma resulting in longer RTHit at the reference grid locations than at other locations in the search area.

Table 2: Repeated Measures ANOVA for 10° search area data for the two analysis methods

Variable	Targ vs Comp		Targ vs Avg	
	F	p	F	p
Metric (M)	63.96	**<0.001***	51.08	**<0.001***
Location (L)	3.71	= 0.053	2.85	= 0.11
Scotoma Size (S)	0.42	= 0.54	0.48	=0.51
M x L	2.24	= 0.16	3.74	=0.64
M x S	4.06	= 0.079	6.24	**= 0.037***
L x S	1.07	= 0.355	1.28	= 0.30
M x L x S	0.55	= 0.54	0.72	= 0.47

Similarities in RTHit results for the different analysis methods can be seen in the results of post hoc analysis on the RTHit data that are listed in Table 3. Paired t-test comparisons revealed that RTHit differences between RTHit values taken at or around the reference target location were significantly longer for all test locations and scotoma sizes than the comparison or grid average RTHit values and this was the case for both scotoma sizes.

Table 3: Ten degree search area Post hoc comparisons for the different test conditions (scotoma sizes and reference locations) and the two methods of analysis

Test Condition (Scotoma size/location)	Targ vs Comp		Targ vs Avg	
	t	p	t	p
1.1°/81	4.4	**= 0.002***	3.4	**= 0.000***
1.1°/13	3.3	**= 0.010***	4.2	**= 0.003***
1.1°/59	3.5	**= 0.008***	3.1	**= 0.014***
1.6°/81	3.8	**= 0.005***	3.8	**= 0.005***
1.6°/13	4.1	**= 0.003***	5.2	**= 0.001***
1.6°/59	4.2	**= 0.003***	3.6	**= 0.007***

Three average RTHit maps for the 1.6° scotoma size at each reference location are shown in Figure 12. The three maps illustrate cases for three different subjects where RTHit was clearly elevated in the vicinity of the grid reference location. In the first map, the grid reference was at location 81, which was above and to the right of fixation and at the intersection of row 4 and column 8 (see Figure 9). As noted previously, across the three search sessions completed per condition, scotoma position relative to the reference was randomly determined and thus could change between search sessions. The result of the position randomization and multiple search sessions was the creation of an area of elevated RTHit around the grid reference that varied in size depending on the exact positions of the scotoma across the three search sessions. This manifests in average RTHit maps that often have rather broad areas of elevated RTHit around the grid reference.

In the first two panels of Figure 12 the peaks are tall and very distinct and cover an area greater than one item location. RTHit maps with this type of feature were common. However, so were maps that had peaks that were more rounded and not as high relative to the surrounding area such as the one in panel three of Figure 12. It is also evident that there are other smaller areas of elevated RTHit throughout the map in panel three. In other words, the surrounding RTHit terrain is not always flat, and in some cases these other peaks were quite high. These anomalies will be discussed in greater detail in the discussion section.

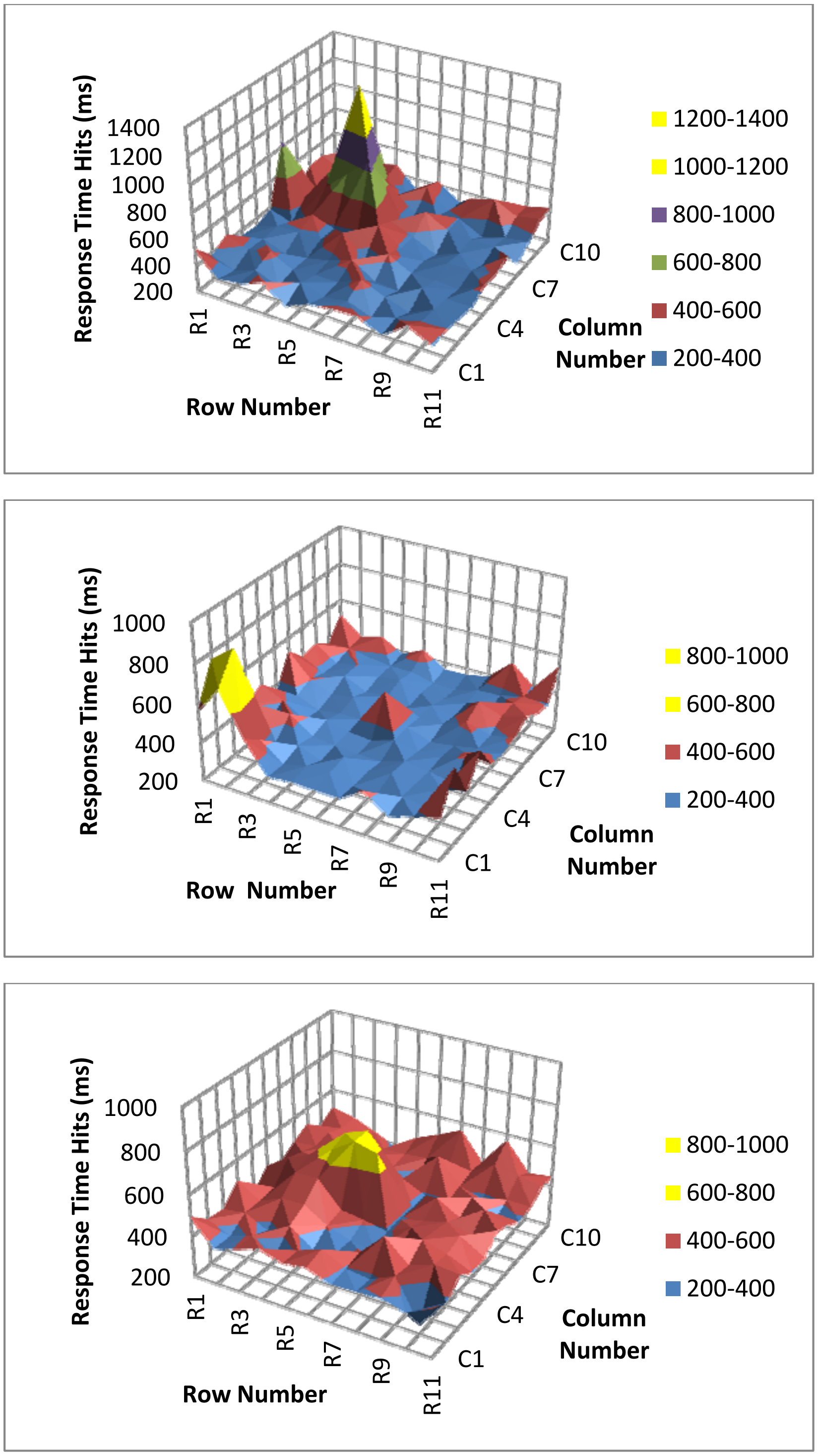


Figure 12: Examples of RTHit maps for the 1.6° scotoma size at target reference locations 81, 13, and 59 on an 11 x 11 grid (see Figure 3). Search area was 10° and data are, in order, from subjects MP, AV, and AS

2.5.1.2 Twenty degree search area results.

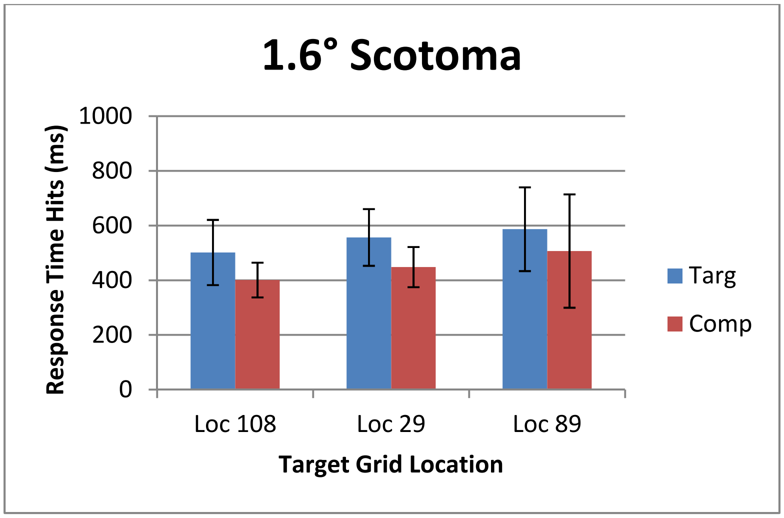
The same general method was used to place the scotoma relative to a target location in the 20° search area. Two of the target locations were similar relative to those used on the 10° search area; one near the upper left corner of the grid and another above and to the right of fixation. The third location was on the vertical meridian in the inferior visual field several degrees above the bottom of the search area. In terms of grid locations, the reference targets were at locations 108, 29, and 89.

The same analysis was used for the 20° search area RTHit data as the 10° data. In the first method, we averaged over the three trial blocks for each subject and compared RTHit for the reference target location (Targ) with RTHit for a target at the symmetrical location on the opposite sides of the vertical meridian (Comp) or in the case of location 89, on the vertical meridian on the opposite side of the horizontal meridian. In the second method, RTHit for the reference target location (Targ) was compared with RTHit average (Avg) for the all locations in the grid.

Table 4 lists the group average RTHit values and standard deviations for the different comparison methods and test conditions. Figures 13 and 14 illustrate the sets of RTHit data from Table 4. Figure 13 shows the differences between RTHit values measured at the reference target location Targ versus the Comp location and Figure 14, Targ versus Avg. Although Targ RTHit values always exceed the comparison and average values, the differences are often not as pronounced as similar comparison in the 10° search area results. Also, the differences for the 1.6° scotoma tended to be smaller than for the 2.2° scotoma.

Table 4: Twenty degree search area average RTHit values for the different scotoma sizes and reference locations for each of the response metrics

Scotoma size/grid location	Targ	Comp	Avg
	RTHit (sd)	RTHit (sd)	RTHit (sd)
1.6°/108	502 (119)	401 (66)	469 (50)
1.6°/29	557 (104)	448 (73)	462 (39)
1.6°/89	587 (153)	507 (207)	468 (53)
2.2°/108	551 (141)	404 (59)	454 (41)
2.2°/29	647 (167)	436 (71)	446 (35)
2.2°/89	656 (173)	449 (157)	453 (72)



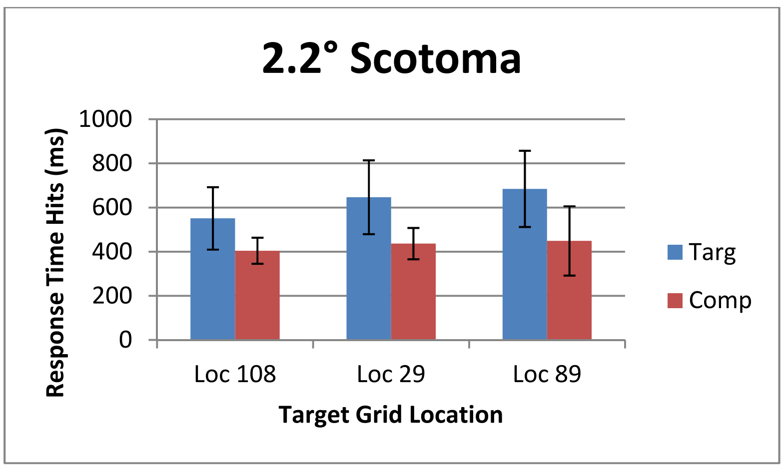


Figure 13: Twenty degree search area, three trial average RTHit for the reference location (Targ), and a comparable (Comp) location in the opposite hemifield as a function of reference grid location for the two scotoma sizes. Error bars ± 1 sd

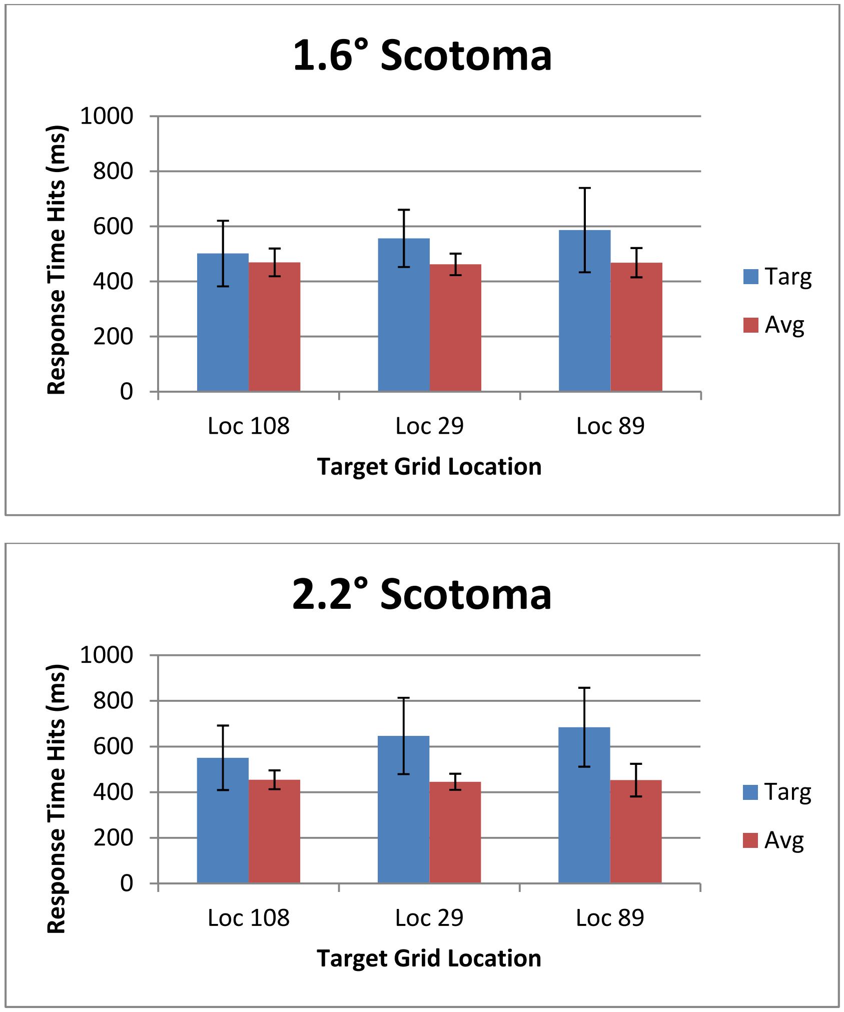


Figure 14: Twenty degree search area, three trial average RTHit for the reference location (Targ) and average RTHit over the block or trials (Avg) as a function of reference grid location for the two scotoma sizes. Error bars ± 1 sd

Repeated measures ANOVA results for the two methods of analysis are listed in Table 5. For both methods, there was a significant effect of the type of RTHit metric and scotoma location but no main effect of scotoma size. The Targ versus Avg method yielded a significant metric by location interaction and both methods yielded significant metric by scotoma size interactions. There were no other significant two or three-way interaction effects.

Table 5: Repeated Measures ANOVA for 20° search area data for the two analysis methods

Variable	Targ vs	Comp	Targ vs	Avg
	F	p	F	p
Metric (M)	13.71	**= 0.006***	16.41	**= 0.004***
Location (L)	7.45	**= 0.01***	4.2	**= 0.48***
Scotoma Size (S)	1.18	= 0.31	3.43	=0.10
M x L	.371	= 0.58	8.26	**=0.005***
M x S	12.0	**= 0.009***	12.34	**= 0.008***
L x S	0.06	= 0.868	0.60	= 0.53
M x L x S	0.65	= 0.48	0.93	= 0.41

Post-hoc analysis using paired t-tests revealed several differences between the two methods of RTHit comparison. For Targ versus Comp, all t-test comparisons were significant except for the 1.6 degree scotoma at reference location 89. In contrast, for the Targ versus Avg, RTHit differences were not significant for either scotoma size at the 108 reference location, although the difference approached significance for the 2.2° scotoma (p = 0.68).

Table 6: Post-hoc comparisons for the different test conditions for the two methods of analysis

Test Condition (Scotoma size/location)	Targ vs	Comp	Targ vs	Avg
	t	p	t	p
1.6°/108	4.3	**= 0.003***	0.9	= 0.353
1.6°/29	4.0	**= 0.003***	2.9	**= 0.020***
1.6°/89	0.9	= 0.382	2.7	**= 0.030***
2.2°/108	2.8	**= 0.025***	2.1	= 0.068
2.2°/29	3.3	**= 0.011***	4.0	**= 0.004***
2.2°/108	3.6	**= 0.006***	4.6	**= 0.002***

Sample RTHit maps for the 2.2° scotoma and three grid reference locations are illustrated in Figure 15. In general, despite statistical significance of RTHit comparisons, the maps for the 1.6° scotoma size were not as clear-cut in revealing RTHit elevations as the 2.2° degree scotoma size maps.

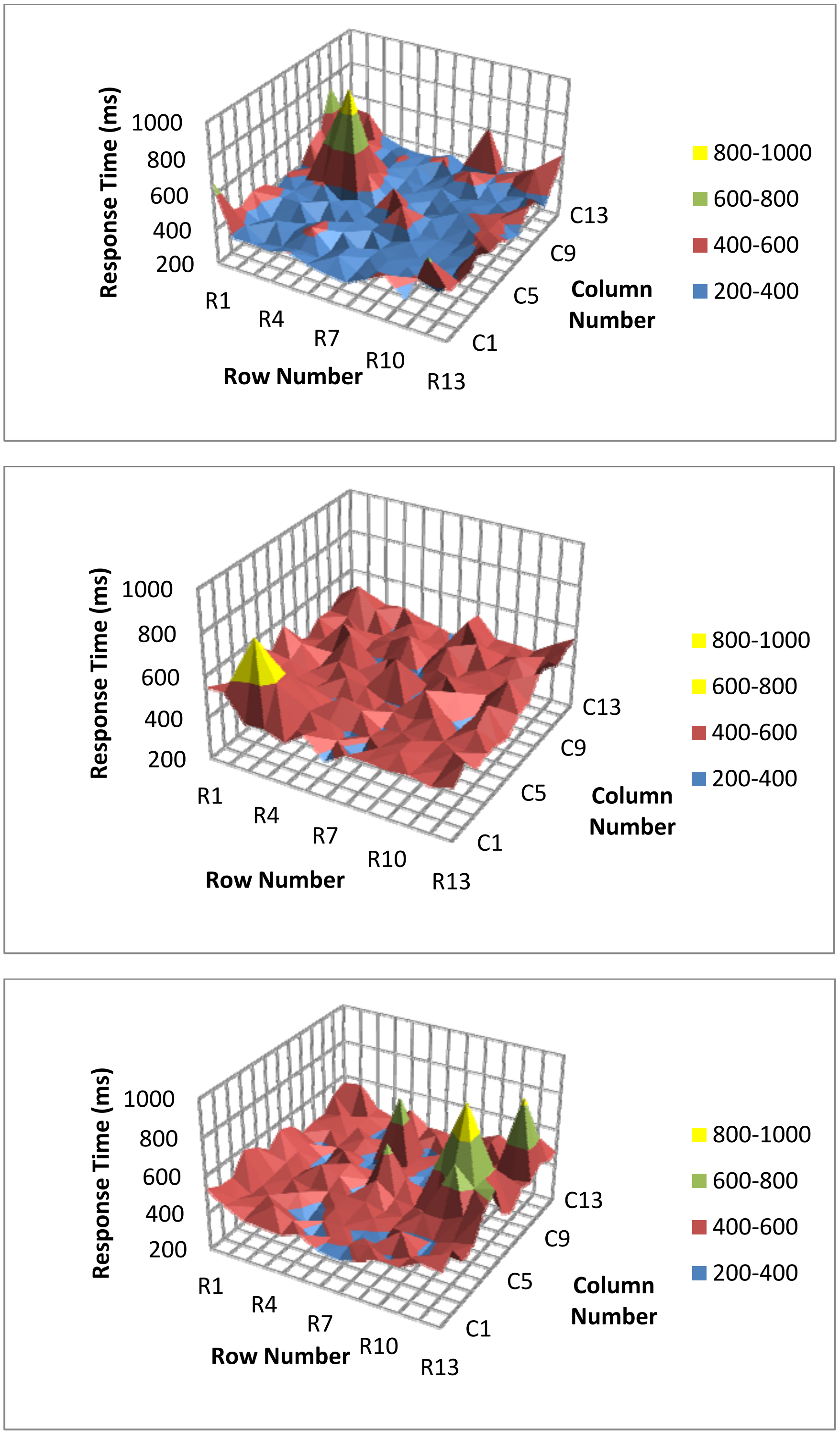


Figure 15: Examples of RTHit maps for the 2.2° scotoma size at target reference locations 108, 29 and 89 on a 13 x 13 grid. Search area was 20° and data are, in order, from subjects MP, AS and SF

3.0 DISCUSSION

Laser injuries often occur in the form of small, punctuate lesions of the retina. Damage to the neural elements that process visual information at the lesion site is likely to result in local changes in sensory visual function. Our hypothesis was that a laser injury that affects retinal function will disrupt visual search and will result in increases in response time for detection of targets imaged on and next to the damaged retinal area. The purpose of this study was to assess the feasibility and effectiveness of a visual search paradigm to address detection of injury to the retina from laser radiation. The results of both experiments support our hypothesis. The general conclusion is that the feature search paradigm can successfully be used to detect small scotoma, on the order of 1.1 to 1.6°, in the central 10° and 20 ° of the visual field, respectively. This is within the size range of laser lesions resulting from moderate burn grade during photocoagulation treatment.[25, 26]

It is probably possible to detect smaller lesions in these search areas, but to do so would require larger grids, more trials, and more time. The 1.1° scotoma detection in the 10° search area required an 11 x 11 grid (experiment 1), 145 trials, and took approximately 5 – 7 minutes to complete. Detecting the 1.6° scotoma on the 20° search area required a 13 x 13 grid, 211 trials, and approximately 7 – 9 minutes to complete. In a field screening setting, these tests would need to be administered to each eye and repeated at least twice. In addition, brief training on the task prior to testing is required. As an example, approximately one hour would be needed to complete testing for the 20° search area.

Experiment 1 was a pilot experiment designed to explore the effects of varying scotoma size and grid size on RT for detection of targets at or near the scotoma location for search areas of 10° and 20° and to determine which test conditions increased RTHit. The results clearly indicated that a scotoma as small as 0.6°, when covering the target (scotoma coincident condition), could be detected in a 10° search area on the basis of increased RTHit. However, when the scotoma were adjacent to the target, scotoma size had to be increased to 1.1° in order to be detected based on criteria of elevated RTHit. Both the 9 x9 and 11 x 11 grid sizes produced equivalent results. For the 20° search area, the 1.1°, but not 0.6°, scotoma could be detected in the scotoma coincident condition with either the 11 x 11 or 13 x 13 grid. However, for the scotoma adjacent condition only the 1.6° degree target could be detected and only with the larger grid size.

Three lines of evidence from experiment 1 suggest that prolonged RT associated with small parafoveal scotoma is caused by one or more eye movements. First, the high hit rate (98%) indicates that the subjects must have moved their eyes. Under most of the testing conditions, the target was either partially or completely obscured by the scotoma at the onset of the stimulus. A high rate of hit responses could not be achieved without moving the scotoma away from the target via eye movements. Second, the RTHit differences between the no scotoma baseline and the scotoma conditions suggest subjects made roughly one more saccade under scotoma conditions than under no scotoma conditions (Figure 4). Third, prolonged RTs were highly correlated with more saccades. It appears that eye movements were purposefully made to reveal concealed targets. During practice trials, subjects quickly learned from auditory feedback that in this search paradigm, not seeing a target immediately did not mean one was not present. The only way to confirm that was by making an eye movement(s). The behavior is reinforced by auditory feedback that signals correct and incorrect responses.

Although the results of experiment 1 confirmed our hypothesis, the experiment was designed to optimize data collection and did not exactly simulate a real-life situation where a scotoma would be fixed in one location on the retina and would always be present. Experiment 2 was set up to do this with scotoma sizes and grid sizes for the 10° and 20° search areas selected based on the results of experiment 1. Three scotoma locations were chosen in order to test different regions of the visual field, and the simulated scotoma were always positioned adjacent to the target since that represented the worst case condition for detection with the visual search paradigm. The scotoma coincident location was not included since the outcome, increased RTHit, seemed obvious from experiment 1, unless the scotoma were significantly smaller than the target.

The results of experiment 2 for the search area indicated that a 1.1° scotoma at all three scotoma locations could be detected on the basis of increased RTHit for the target location that served as the reference for positioning the scotoma compared to symmetrical target locations, or the average RTHit for a block of trials. The larger 1.6° scotoma yielded longer RTHit for the target reference location and larger differences compared to RTHit for the symmetrical location. In other words, the larger scotoma size data were more clear cut. For the 20° search area, the results indicated that the 2.2° scotoma was detectable at all three locations using the Targ versus Comp analysis method.

Although the results of both experiments indicate that using feature search for scotoma detection is feasible, the data tended to be noisy. The issue is the presence of abnormally long RTHit times at target locations that are removed from the scotoma location. However, this phenomenon is not unique to feature search but also occurs during perimetry and there are ways to address it. An example is shown in Figure 16 for the 10° search area and grid reference location 13 (upper left corner) for the 1.6° scotoma size. In addition to the RTHit peak at the reference location, there is another peak to the right and also an area of increased RTHit in the center of the map. This type of pattern with multiple peaks was relatively common, more so for the 20° search area data. In a screening situation, the test is likely to be administered one or two times and scotoma location will not be known. Therefore, a method for eliminating what appear to be spurious data points and identifying where the scotoma is located needs to be implemented.

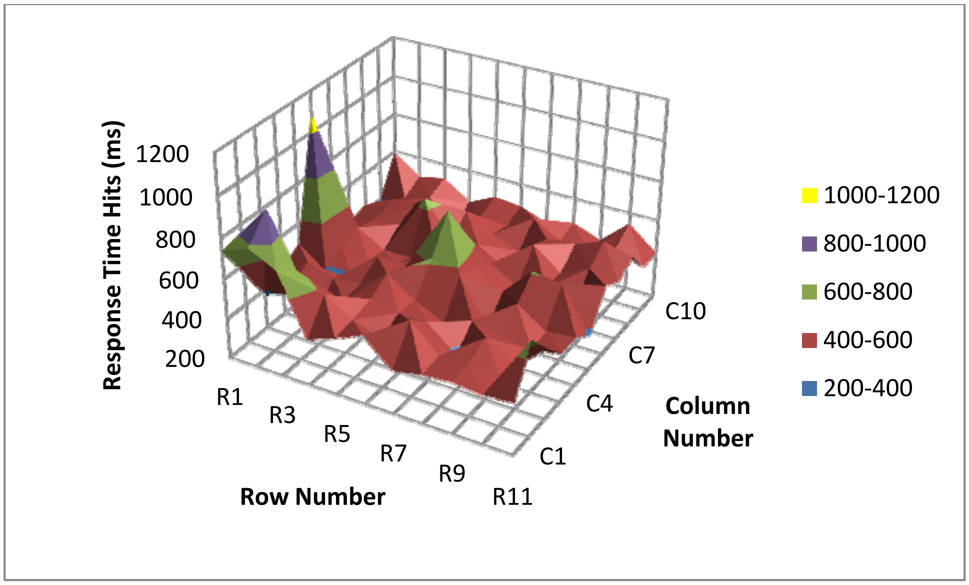


Figure 16: RTHit map for one of the trial blocks from the Average RTHit map for subject AS shown in Figure 10 for the 1.6° scotoma size at target reference location 13

One approach is to re-test at suspicious locations. Examination of several sets of RTHit data for single blocks of trials indicated RTHit outliers occurred between 2 and 6 times per search session. They are most likely the result of lapses in attention by the subject. In addition, false positives constitute only 1.6% to 5% of total number of trials for a 11x11 grid and 1.2% to 3% of total trials for a 13x13 grid. That means that after a first round of testing, there is only a very small portion of suspicious locations that need to be retested, which will only slightly increase the testing time, but will greatly increase the test accuracy. Given computer processing speeds, computation of average RTHit and standard deviation (sd) and re-testing of suspect locations where RTHit exceed some (sd) criterion could be accomplished in a seamless manner without subjects being aware they are receiving additional trials. The same strategy is also used in single-intensity suprathreshold screening using a static perimeter. Considering the observed low rates of RTHit outliers and false positives, the retest should converge on the true scotoma very quickly. If 6 false positive locations are identified on a 11x11 grid, the chance of producing one or more false positive in the first round of retesting of the 6 locations is low. Future development of the feature search test will be focused on the algorithm to detect the suspicious locations for retesting. One approach is to calculate the average RTHit and standard deviation (sd) at the end of a search session and re-test those locations where RTHit values exceed some sd criteria (e.g > 2sd above the mean). At the same time, any clustering of long RTHit at specific locations, which may be indicative of a scotoma affecting multiple grid loci, can be taken into consideration for re-testing. One question is how many times to re-test a location in order to decide to reject an abnormally long RTHit. Another is where to set the re-test criterion, and a final question is how successful is this process at minimizing noise in the data set.

A limitation of the method we used in experiment 2 was the randomization of the reference target position relative to the scotoma position. In real-life, there would be only one scotoma location. In a screening scenario it is likely that the test would be repeated at least twice. In a situation where the scotoma does not lay on top of one grid location, then over several repeats of the test, an area of elevated RTHit encompassing multiple grid locations adjacent to the scotoma, should emerge. Although scotoma location was fixed during a block of trials and we have examined and analyzed several single trial blocks, it would be useful to have an idea of how many repetitions of the test might be needed to obtain a clinically useful result. By randomizing scotoma position relative to the reference location across trial blocks, we cannot assess the true impact of repeating trial blocks. In future experiments, scotoma position could be fixed across trial blocks, its location recorded, and the results of multiple test repeats compared to a single block of trials.

The present study used achromatic contrast as the primary stimulus feature. Several color conditions (not reported) were tested, and they yielded very similar results. Although the contrast feature worked well, it may be that a greater contrast difference between targets and distractors, to further increase feature salience, or using other stimulus features such as size or shape might yield even better outcomes. Also, a very sparse item density of 20% of the total number of positions in a grid was used. That decision was based on some observations during set-up and system and software testing that suggested a sparse density of items produced more uncertainty and might yield better results. However, item density was not systematically varied, and it is another factor that could be investigated.

Test time may be viewed as a potential limitation of the search paradigm, but perimetry has the same issue. Like perimetry, the search test requires more trials to detect smaller scotoma over a given area. However, because feature search is likely to produce more reliable results, as we argued in the introduction, more time can be saved in rechecking suspicious locations. With the 13 x 13 grid and over 200 trials in a test session, total test time was 7-9 minutes. This is relatively short compared to some visual field testing methods. Another issue search shares with perimetry is that the task, although simple, is monotonous in its repetition. In our test situation, this may have been exacerbated since subjects repeated many blocks of trials over all of the test conditions over the course of several days of testing, with test sessions lasting an hour or more. As noted previously, this may contribute to attention lapses and the occasional abnormally long response times. This will likely be less of a problem in a field test setting where subjects complete several repetitions of the test for each eye and are finished. Furthermore, for naïve subjects search may actually be the more interesting task because they get to see targets pop out.

The feature search task requires some training/practice in order for subjects to gain stability in response times.[21, 22] In the practice and test sessions of the current study, feedback on response accuracy was given. The implications of feedback in a field test is that it may be required if RTHit is to be the primary outcome measure. This would require a training session with feedback prior to testing and then feedback during testing to reinforce the behavior of making eye movements when a target does not immediately pop out. The alternative is to provide no feedback. If this is done, missed responses are very likely to increase, and they would need to be taken into account, along with increased RTHit, as important indicators of scotoma presence.

Which method produces the best results is not clear, although in terms of data noise reduction strategies, locations where misses or RTHit above a threshold would be targeted for re-testing. Regardless, some training on the task is required, and it can be as easily done with feedback as without.

Subject perceptions of scotoma presence and shape were similar for experiments 1 and 2. In experiment 1, subjects did not report being aware the target was always paired with a scotoma. This is likely due to several factors. One was sparse item density which left most of the area being tested devoid of any visual stimuli that could aid in defining scotoma location. Another was that subjects were focused on finding the target, not looking for a scotoma. In addition, the 25% negative trials were sufficient to keep subjects uncertain about target presence or absence and focused on the task. In some pilot experiments with a high item density, large scotoma could be clearly seen and changes in position observed with eye movement. Similarly, in experiment 2 subjects generally did not report knowing where exactly a scotoma was located even though one was always present in the same location during a search session. Again, sparse item density and focus on the task which was locating targets that could appear anywhere in the search area, occupied subject attention. In addition, during repeat search sessions under the same test conditions, the scotoma were likely to be located at one of the other four possible positions around the grid reference, further adding to some uncertainty about its exact locations. Subjects occasionally reported in experiment 2 that they thought they knew where scotoma had been located but even then their judgments were rather vague, e.g., "somewhere above and to the left of fixation." Subjects also did not comment on scotoma structure – fuzzy or distinct borders, circular in shape, except in pilot studies with high item densities and then the scotoma did appear distinct, circular in shape and with fuzzy borders.

We also hypothesized that because visual search is a simple task to perform it can be done successfully even in the presence of significant retinal injury. The latter claim was based on success using a feature search paradigm in persons with severe to profound visual impairment. [22-24, 31] Our experiments are among the few that have investigated the effect of parafoveal scotoma on functional visual performance. Like a central scotoma which clearly impairs visual performance, [8-10; 27-29] our results indicate that a relatively small parafoveal scotoma can also have a significant impact. Searching the environment for items of interest is a continually occurring visual event, for example, searching for obstacles and landmarks while walking or driving. Visual search was clearly slowed by the presence of scotoma and our findings represent a new and important contribution to the literature on the effects of sight loss in peripheral vision.

Exploring an alternative strategy to improve detection of scotoma in a shorter period of time may be to use a multiple-target presentation paradigm. This can be implemented where multiple targets (1-4) are briefly presented at any given time in a relatively restricted area within the visual field such that focal attention rather than more global attention is used. Previous studies of multi-target perimetry tended to spread targets over large area and the results were not always successful as a visual field assessment. In multi-target presentations, the subjects' task is to identify the number of targets presented. Subjects are generally very good at this task provided the number of targets presented is small and as noted, not scattered over a large area. Knowing the number of targets presented to focal attention does not require scanning and seems to occur instantaneously.

4.0 CONCLUSION

In summary, the feature search method is a feasible approach to scotoma detection. However, to validate and optimize the technique, several avenues need further exploration. The first is to evaluate the paradigm with the scotoma fixed in one location in the search area and to test monocularly. Although binocular presentation in the present study was a valid approach to demonstrate feasibility, in field testing it would be necessary to do the test for each eye. The second is to develop strategies to re-test locations where RTHit values exceed some criterion, similar to methods used in automated perimetry when suspicious data points occur. A third is to determine the impact of repeated tests with the scotoma fixed in order to provide some guide to using the test in a field situation. A fourth is to determine if giving feedback on response accuracy is a better strategy than not giving any feedback.

This feasibility study demonstrated that a feature search paradigm can successfully be used to detect relatively small simulated retinal lesions in central vision. However, more research is needed to get the methodology to the point of being used for laser injury screening in the field.

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